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CONDUCTED BY

G. M. HUMPHRY, M.D. F.R.S.
PROFESSOR OF ANATOMY IN THE UNIVERSITY OF CAMBRIDGE,
HONORARY FELLOW OF DOWNING COLLEGE;

WM. TURNER, M.B. F.R.S.
PROFESSOR OF ANATOMY IN THE UNIVERSITY OF EDINBURGH;

MICHAEL FOSTER, M.D. F.R.S.
PRÆLECTOR IN PHYSIOLOGY IN TRINITY COLLEGE, CAMBRIDGE;

WM. RUTHERFORD, M.D.
PROFESSOR OF THE INSTITUTES OF MEDICINE IN THE UNIVERSITY OF EDINBURGH.

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ON THE DEVELOPMENT OF THE MAMMA AND OF THE MAMMARY FUNCTION. By CHARLES CREIGHTON, M.B. (Pl. I.)

THE current and at present unchallenged opinion on the development of the breast is that it is a complex extension downwards of the ectoderm. From observations made chiefly on the human fœtus, it is said to begin, in the fifth month of fœtal life, as a solid rounded process of the *rete mucosum*; before the seventh month, this wart-like body has thrown out 12 to 15 offshoots from various points of its circumference. From that rudiment, the whole complex structure of the gland grows out by a process of continuous extension. The rudiment of the gland is at first solid, and the formation of cavities throughout the various extensions of the rudiment is associated with the formation of fat-containing cells in their interior. These fat-containing cells, by means of which the channels of the gland are formed, constitute the milk of the new-born, which is therefore a developmental product[1].

The development of the mamma is thus held to be a process of budding from the mucous layer of the skin, and the homology of the organ is always sought for in other accessory cutaneous glands, and chiefly in the sebaceous glands. Fully accepting that homology, Mr Darwin has cursorily applied the principle of natural selection to explain the adaptation of the breast as a mammalian characteristic, and Mr Mivart, joining issue on this illustration, has suggested whether "it is conceivable that the young of any animal was ever saved from destruction by accidentally sucking a drop of scarcely nutritious fluid from an accidentally hypertrophied cutaneous gland of its mother[2]."

[1] Kölliker, *Entwicklungs-geschichte*, 1st Edition, p. 345.
[2] See *Origin of Species*, 6th Edition, p. 189.

The biologists of the Jena school have also confidently accepted the same view of the homology of the breast.

It is somewhat startling to find, on making inquiry, that the notion of the mamma being a continuous extension downwards of the skin, and the important doctrine of homology that is based thereon, are supported by the most meagre and unsifted evidence. The first statements on the development of the breast appear to have been made by Kölliker, in an early edition of his work on Histology, and these original statements have determined the character of all subsequent opinion. The view therein given is substantially the same as that already quoted from his work on Development. Within a short time of Kölliker's first reference to the subject, a memoir on the human breast was published by Langer[1], in which he gave an account of the development. The statements of Langer, to be shortly referred to, were held by Kölliker to be in agreement with his own; and in the great work of Remak, Kölliker and Langer are quoted together, and without distinction, as having shown that "the mammary glands, like the sweat glands, are formed from the Malpighian layer of the upper skin[2]." There has thus arisen an apparent unanimity as to the development of the mamma by outgrowths from the ectoderm, and that view passes unquestioned at the present time. Notwithstanding, the conclusion of Langer, in his own words, is: "The first development of the mammary gland is thus associated with the existence of a peculiar, independent body (*an die Existenz eines eigenthümlichen, selbständigen Körpers gebunden*), in which the ducts develope without connexion with the groove in the skin, and are therefore not invaginations or processes of the outer skin (*somit keine Ausstülpungen oder Fortsetzungen der äussern Haut sind*)."

The plan according to which most of the secreting glands of the body, including the breast, are supposed to develope, is that the rudiment commences as a downward process of the epithelial surface on which the gland, in its mature state, will pour its secretion. The gland is essentially a very complex reduplication of the epithelial surface. The development of the gland,

[1] *Denkschriften der Wiener Akademie*, 1852.
[2] *Untersuch. über die Entwickl. der Wirbelthiere*, p. 100.

according to this view, may also be said to be centrifugal; the growth takes place by the throwing out of processes from a central point of the surface towards a wide periphery at the depth. The botanical terms of "bud," "offshoot," &c., are constantly used to describe the process of formation of a racemose gland. The structural growth, however complex, is held to be one of continuous extension downwards, just as the growth of a plant is into the air upwards. The ducts of a gland grow like the branches, and the acini unfold like the leaves. But it is a remarkable abuse of terms to transfer, in so facile a manner, the language of plant-growth to the growth of a racemose organ within the body. The continuous extension that can be observed in a growing plant, cannot be observed in the microscopic preparations of a developing gland. However commonplace this remark may be, there is reason to think that writers on development have not always respected the difference between the facts derived from immediate observation and the facts derived from mediate evidence. In the microscopic examination of dead tissues one never observes anything but coexistences, but in our descriptions we use the language of succession; and, even if no fallacies have crept in through such laxity of expression, the evidence, which is needed to make the mediate truth of the same value as the truth of direct observation, is apt to be deficient.

Although the doctrine of continuous extension from a central point on the surface has been accepted without challenge[1],

[1] A modification of this view has lately been put forward by Schenk. In an original investigation on the development of the pancreas, he draws a distinction between the source of the secreting cells of the organ, and the epithelial lining of the ducts. He derives the former from the mesoblast, and the latter from the hypoblast (*Die Bauchspeicheldrüse des Embryos*, *Anat. u. Physiol. Untersuch.*, quoted in Foster and Balfour's *Embryology*, p. 133). In his *Lehrbuch der Vergleichenden Embryologie der Wirbelthiere*, the same author states this opinion more generally. Speaking of the development of glands connected with the epithelial-glandular layer he says: "Wir müssen hier gleich anfangs darauf aufmerksam machen, dass man die Anlage der sogenannten Darmdrüsen, deren Entwicklung nach Remak im innern Keimblatte stattfindet, nicht im Sinne der älteren Autoren auffassen kann, dem zufolge die einzelnen Anhangsorgane des embryonalen Darmes, wie Lunge, Leber, &c., Ausstülpungen des Darmkanals wären. Vielmehr sieht man sich genöthigt, an diesen sämmtlichen Organen nur insoferne das Darmdrüsenblatt als betheiligt anzusehen, als diess blos Epithelialgebilde, für die Auskleidung der einzelnen Ausführungsgänge oder deren Verzweigungen abgiebt. Die Elemente, welche das Parenchym dieser Organe ausmachen, werden zumeist der Urwirbelmasse entnommen,

an entirely different account of gland-development was put forward in 1842, by John Goodsir. These remarkable and far-reaching views of Goodsir can hardly be said to have gained currency, no doubt owing to the aphoristic manner in which they were expressed. They are for the most part stated in naked propositions, without the support of the laborious details on which they had certainly been based. Goodsir's statements are as follows[1]: "The blastema, which announces the approaching formation of a gland in the embryo, in some instances precedes, and is in other instances contemporaneous with, the conical blind protrusion of the membrane upon the surface of which the future gland is to pour its secretion.

"In certain instances it has been observed that the smaller branches of the duct are not formed by continued protrusion of the original blind sac, but are hollowed out independently in the substance of the blastema, and subsequently communicate with the ducts.

"It appears to be highly probable, therefore, that a gland is originally a mass of nucleated cells, the progeny of one or more parent cells; that the membrane in connexion with the embryo gland may or may not, according to the case, send a portion of the membrane, in the form of a hollow cone, into the mass; but whether this happens or not, the extremities of the ducts are formed as closed vesicles, and then nucleated cells are formed within them, and are the parents of the epithelium cells of the perfect organ." These summary statements are prefaced by the remark: "We require renewed observations on the original development of glands in the embryo. From the information we possess, however, it appears that the process is identical in its nature with the growth of a gland during its state of functional activity." It is the latter subject that chiefly engaged Goodsir's attention. His observations were made on animals in which the glands have particular periods of functional activity. Certain glands in crustacean animals and the sexual glands of

welche den Darmkanal umgiebt," pp. 88—90. Although Professor Schenk here speaks of the doctrine to which I have referred in the text as being the view taken by "the older authors," the newer school appears to be represented chiefly by Professor Schenk himself. Perhaps his language is only a confident anticipation of the future.

[1] *Anatom. and Path. Observations*, p. 32, 1845; also collected Anat. Memoirs.

some vertebrates were studied during those periodical processes of "development, maturity and atrophy," which they undergo from season to season; and it is with those periodical processes that he says the embryonic development is identical. The great significance of this remark will be discussed at the end of the present paper; but a short extract at the present stage will be useful to illustrate further Goodsir's view of the embryonic development of acini. The above-quoted statement that "the extremities of the ducts are formed as closed vesicles" will become clearer from the following, relating to the periodical "development": "An acinus is at first a single nucleated cell. From the nucleus of this cell others are produced. From these again, others arise in the same manner. The parent cell, however, does not dissolve away, but remains as a covering to the whole mass, and is appended to the extremity of the duct. Its cavity, therefore, as a consequence of its mode of development, has no communication with the duct.

"The original parent cell now begins to dissolve away, or to burst into the duct at a period when its contents have attained their full maturity. This period varies in different glands, according to a law or laws peculiar to each of them.

"In the gland, there are a number of points from which acini are developed, as from so many centres. These I name the germinal spots of the gland."

The following account of the development of the mamma in the guinea-pig will be found to support Goodsir's general view of gland-development. The agreement with Goodsir's doctrines was not observed till the conclusions of the present research were in great part formed, and, indeed published in the form of a preliminary notice[1]. Goodsir's philosophical generalisations on secretion and on the secreting structures do not appear to be generally taught by the present school of physiologists either at home or abroad. Whether it is from the comparative neglect of cellular processes on the part of physiological teachers, or whether it is from the brevity of Goodsir's statements, or from both circumstances combined, it is doubtful whether the latter, even when the attention

[1] Physiological Processes of the Mamma, Section IV. in the *Report of the Medical Officer of the Privy Council*, 1875.

is especially directed to them, would not remain somewhat enigmatic to any one who had not been independently led to follow the same line of inquiry.

In the new-born guinea-pig the mamma is found in the inguinal region on each side, extending obliquely downwards and backwards from the single nipple. If a vertical section is made in a line running from the nipple inwards toward the symphysis pubis, the tract of mammary tissue is exposed. In a preparation hardened in alcohol it appears as a somewhat narrow strip of whitish tissue about half an inch in length and running through the midst of a large body of fat-tissue. From the long central tract, short and inconspicuous offshoots project into the surrounding fat.

In embryos about two-thirds grown, the mammary rudiment is found to have the same relative position and extent. In the section of the prepared tissue there is not the same naked-eye distinction between the tract of mammary tissue and the surrounding fat. Mamma and fat together form a small pear-shaped body beneath the skin, the narrow end terminating anteriorly at the nipple.

At both of the stages here mentioned, the developing mamma is found to have relatively its full dimensions, and to lie amidst a quantity of fat-tissue; the plan of the organ is, as it were, laid down over its whole extent. In the earlier of the two stages, the acini have not begun to appear distinctly, but only the system of ducts. At the time of birth, however, the acini are found in active development, and within a few days after birth they are sometimes found to have so great an expansion as to completely overshadow the system of ducts.

The development of the system of ducts can be best considered after that of the acini has been described, for reasons that will appear. The contention of the first part of this paper is that the acini, or essential secreting structure of the breast, develop from a matrix-tissue at numerous scattered points or centres ("germinal spots" of Goodsir); that the matrix-tissue or embryonic cells are the same from which the fat surrounding the mamma developes; and that the mode of development of the acini is, for the individual cell, exactly the same process as in the development of the fat-lobules.

The mammary gland would therefore be a further specialisation of fat tissue, and a product of the mesoblast. It has been said that the opinion of the mamma being a complex extension of the ectoderm has gained currency in a remarkably easy and undeserved manner, and that a sufficient proof of this process of extension from the skin would be really a very arduous matter. But if it is difficult to prove that origin of the mamma by direct evidence, it is no less difficult directly to disprove it. To make out a parallelism, however, between the development of the mammary acini and the development of the adjacent lobules of fat is perfectly fresh ground; and that parallelism, and the identity of the matrix in the two cases, will be the issue raised.

The resemblance between the mode of origin of the fat-lobules and of the mammary acini is first suggested by that stage of the development of the breast which is represented in Fig. 1. The figure represents a mammary lobule in a guinea-pig four days old. The expansion of the lobule is very considerable, so much so that the system of ducts is completely obscured by the acini. Each acinus is a rounded space distended by large vacuolated cells like fat-cells, among which many nuclei lie at various depths. If reference be now made to Fig. 2, which shows the condition of the breast in the guinea-pig three or four weeks earlier, some idea will be obtained of the way in which this great expansion of secretory structure comes about. In the earlier of the two stages of development, there are present only the ducts, representing the framework of the gland, and around them a quantity of embryonic tissue. It is from this field of embryonic tissue that the cluster of acini, as shown in Fig. 1, have sprung up. Now, at the earlier stage of development shown in Fig. 2, a development of the matrix-cells into fat-cells has already taken place at various points; the space immediately surrounding the rudimentary lobule in the figure is occupied by fat-tissue, although the drawing has not been extended so far. It will thus appear, that if the mammary acini and the fat-lobules that surround them develop from the same matrix, the fat-development is about three weeks in advance of the development of the secreting structures. The contention is that the

embryonic tissue nearest to the ducts is left to undergo a later and somewhat more special differentiation.

It might therefore be supposed that the mammary region of the guinea-pig contained within itself, at various periods of embryonic life, all the elements for a comparison between the development of collections of fat-cells and the development of acini. The assertion is that from one and the same matrix there develop first a certain number of fat-lobules, and afterwards the acini. The peculiar cellular transformation that leads to the production of fat-lobules in certain parts of the matrix is the same that, three weeks later, leads to the formation of acini in the surviving or untransformed part of the matrix. But that apparently simple question cannot be put to a satisfactory proof in the guinea-pig alone. It so happens that the parallelism between the fat-development and the development of acini can be much more clearly traced by studying the course of fat-development in the inguinal region of the fœtal kitten; and the reason of this will now be explained by a statement of the anatomical characters of the mamma in the two animals.

In the adult guinea-pig the mamma on each side is a flattened pyramidal body, the apex of which is at the nipple and the base towards the groin; its length is rather more than one inch. The mammary structure proper is of a reddish brown colour, and is surrounded on all sides by a large quantity of fat. In a vertical section of the entire organ, including the fat, the brownish parenchyma of the gland appears as a central wedge, sending out processes into, and interlocking with the fat on all sides. The mamma is not separable from the fat without much dissection, but the mamma and fat together form a flattened pyramidal mass which is loosely connected with the surrounding tissues. On the other hand, the mamma of the cat on each side is an extensive broad and flattened strip of glandular substance extending from the groin to the upper part of the thorax, and supplied with four or five teats at intervals corresponding to the systems of ducts of four or five originally separate glands. It is only at the inguinal end that there is a considerable quantity of fat; it forms a thick cushion beneath the gland. The mamma is an expanded

layer or stratum of purely glandular structure, which rests, chiefly at its inguinal end, upon a cushion of fat. Whereas in the guinea-pig the fat could be separated from the gland only by a tedious dissection, in the cat it could be removed by a single horizontal incision.

Corresponding to those anatomical differences in the adult condition of the two animals, there are remarkable differences in the development. What may be called the mammary fat develops in the kitten not only in the plane beneath the mamma, but it develops as an independent *organ*. This organ is a *fat-body*, not differing, except in its ulterior development, from the fat-bodies that occur in other classes of animals in various situations and possessed of various functions. But there is another important difference between the mammary fat of the kitten and that of the guinea-pig. In the fœtal guinea-pig the fat has passed through its embryonic transformation and has reached its nearly perfect or mature form about three weeks before birth. In the kitten the fat, developing as a fat-body, is still undergoing its developmental changes up to, and in some cases a few days beyond, the time of birth. The development of the mammary fat is a very much slower or more gradual process in the kitten than in the guinea-pig. From this circumstance, and from the circumstance of its development as a separate organ or fat-body, or rather from both circumstances inextricably combined, the comparison can be best made between the mammary fat of the kitten, on the one hand, and the acini of the guinea-pig on the other. An interval of about three weeks occurs in the guinea-pig between the fat-development and the formation of the acini, and the same interval of time occurs between the completion of the fat-development in the guinea-pig and that in the kitten; so that, although the mammary acini in the new-born guinea-pig are comparable to its fat-lobules three weeks before birth, they are also comparable to the fat-lobules of the kitten of its own age; and that comparison is much the more striking of the two. There is reason to think that the development of the mammary acini in the kitten follows that of the fat-lobules by about the same interval as in the guinea-pig, and that it takes place on the upper surface or

youngest part of the fat-body; but the development of the acini will be explained in the guinea-pig only. The kitten will therefore be used to explain the fat-development in the inguinal region, and the guinea-pig to explain the mammary development; and it will be most convenient, in order to make a comparison between the two processes, to commence with an account of the former.

The description now to be given of the development of the fat-tissue in the inguinal region of the kitten, or, in other words, of the inguinal fat-body of the kitten, does not differ essentially from that given by Toldt[1]. The chief points of immediate interest in Toldt's paper are as follows. In the earlier months of embryonic life the fat-cell is a round and finely granular cell with a nucleus, but without a cell-wall, and differing from a colourless blood-corpuscle only in point of size; at this stage the fat-cell is already differentiated from a connective-tissue cell. The development of the fat-tissue is always directly bound up with the existence of a system of blood-vessels; if three or four cells are found grouped together as the rudiment of a fat-lobule, this grouping is already in connexion with blood-vessels. By reason of the characteristic and independent system of blood-vessels for the fat-tissue, there is suggested a close analogy between the aggregate of fat-lobules and an acinous gland[2]. Those aggregates of fat-lobules are the fat-bodies. It is in the form of independent organs that the future fat-tissue occurs in the embryo stage of some mammalians, while these bodies persist through life in batrachians. In insects, they are organs of great importance, and of various functions. The fat-body in the inguinal region of the new-born kitten is one of those described by Toldt; one of the figures in illustration of his paper gives an excellent idea of the perfect and independent vascular supply of the fat-body.

The pair of fat-bodies in the inguinal region of the new-born kitten are at first sight exactly like a pair of secreting glands. They are about half an inch in length, somewhat

[1] *Sitzungsberichte der Wiener Akademie*, 1870, p. 451.

[2] Professor Toldt's words are: "There can be no more perfect analogy than that which subsists between the fat-tissue and the so-called acinous glands in respect of the distribution of their blood-vessels."

curved, and placed with their convexities towards the middle line of the body; their posterior end is thick and rounded, and anteriorly they become narrower and pointed. Their anterior ends at the time of birth correspond almost exactly to the inguinal pair of teats of the kitten. The blood-vessels may be seen ramifying on their lower and flattened surface, a large trunk running exactly in the centre from behind forwards, and giving off branches symmetrically on each side. The bodies have a loose fibrous investment, which isolates them throughout most of their extent; but at the upper and anterior end they cannot be detached without some tearing of their substance. In other words, their anterior extremity is not definitely rounded and circumscribed as the posterior is. They have the parenchymatous consistence and pinkish colour of a secreting gland, when fresh; after hardening in spirit, they become more spongy. Microscopic sections of them present a very beautiful appearance. The lobules are large at the posterior end of the body; the smallest groups of cells are met with at the upper and anterior end. Each lobule is a closely packed mass of large cells with very striking characters (Fig. 3, C). The substance of the cells is a granular protoplasm, and in all of them it is occupied by one or more vacuoles. Generally there is only one large vacuole occupying the lower segment of the sphere, while the protoplasm is chiefly massed at the other pole of the cell, and appears in section as a crescentic band. The nucleus has usually an excentric position in the midst of the crescent-shaped band of cell-substance. The boundary of the cell, or the wall of the vacuole, is also formed by the same granular substance, forming a narrow belt or ring at the opposite pole. These cells have all the character of secreting-cells; if there was an outlet for their fluid contents, the fat-body might be viewed as a gland. But a few days after birth, this developmental appearance passes away; the cells of the fat-body are so completely excavated and filled with fluid that their granular substance disappears, and the original protoplasmic cell is represented only by a thin sac-like membrane filled with an oily fluid. Instead of the vacuolated cell giving up its fluid contents, as in a secretory process, it retains the fluid

permanently. At the same time the individual cells expand greatly, and the fat-body becomes a mass of fat which extends forwards and laterally.

Many of the cells found within the developing acini of the mamma (in the guinea-pig) have the closest resemblance to the vacuolated protoplasmic cells of the fat-body (in the kitten), and this resemblance is so striking, that, in the preliminary notice of this investigation, it was said that the upper and younger groups of cells of the fat-body in the kitten did actually become the acini of the mamma. That, however, is too superficial a view of the problem, and cannot be shown to be true as a matter of fact. There is not an identity between the fat-body, or any part of it, and the mammary secreting structure; but there is an identity in the matrix-tissue of both, and a remarkable parallelism in their respective developments. This parallelism will now be explained, first by tracing the fat-body (of the kitten) backwards to its origin, and afterwards by describing the mode of origin of the mammary acini (in the guinea-pig).

The various representative stages of the fat-body are shown in A, B, and C of Fig. 3, that shown in C having been just described as the stage immediately preceding the final or mature stage of the fat. The condition in B, taken from an embryo kitten about 3½ inches long, or two-thirds grown, is the characteristic earlier stage; while A, from an embryo kitten 2½ inches long, shows the earliest collection of cells that can be identified as going to form a fat-lobule. The fat-body, which, at the acme of its development, is an isolated parenchymatous organ with a separate vascular supply, commences at many scattered points in the inguinal region. The small groups of cells that afterwards become fat-lobules first show themselves at the extreme inguinal end of the abdominal wall. Between the abdominal muscles on the lower side and the rete mucosum on the upper, a wedge-shaped mass of gelatinous tissue is inserted, the pointed end being forwards. It is in this subcutaneous matrix that the clusters of fat-cells take origin. The appearance of this matrix-tissue is shown in Fig. 3, A. Spindle-cells occur somewhat sparsely in the midst of a ground-substance which is hyaline when fresh, but

assumes a granular or thready appearance after coagulation by reagents. At an earlier period, the embryonic cells of this region are relatively much more numerous. The spindle-cells are the ordinary embryonic cells of the mesoblast, persisting to a comparatively late period of fœtal life. At a number of points, such as the one shown in the centre of the figure, cells are massed more closely. There is no reason to suppose that these groups of cells are derived from any other source than the spindle-cells of the part. The group begins to form by the subdivision of one of the embryonic cells; the progeny are more globular, and with a larger amount of protoplasm round the nucleus. The differentiation towards a fat-lobule has already begun, and the divergence from the spindle-cell or cell of the connective-tissue type goes on increasing. The small clusters of spherical protoplasmic cells expand; the cells at the same time become larger and more like epithelium, the growing lobule having the appearance shown in Fig. 3, B. In the oldest part of the fat-region, the lobules are already large and packed closely together; although the fat-body is not yet encapsuled or isolable as whole, yet the space between the rete mucosum and the abdominal muscles is readily seen to be occupied by a special kind of tissue, forming a wedge-shaped mass which, in alcohol preparations, has a whitish appearance. The largest lobules are many times the size of the one figured, and their cells, representing a passing phase in the development, often have a close resemblance to the epithelial cells of the supra-renal body. About the time of birth the fat-body has acquired the appearance of being an independent organ, and the cells are all vacuolated as in Fig. 3, C. During the development of the fat-body, one or more lymphatic glands have developed apparently in the midst of it, towards its lower surface.

Throughout the growth of this body or organ, the development, as has been already stated, is not in an equally forward state at all points. The groups of fat-cells first appear at the extreme inguinal end of the region, and the order of appearance of the various centres of development is, throughout the whole process, from behind forwards and from below upwards. Again, when the fat-bodies are already of considerable

size in the groin, the corresponding formation of fat-tissue at separate points, beneath the three or four anterior pairs of teats in the kitten, has not advanced beyond the first stage of small scattered groups of embryonic cells. In these anterior regions of the abdominal and thoracic walls, the fat is at no period of its existence found as a separate body or organ, although the early stages of its formation are the same as in the actual fat-body of the groin. Limiting the attention again to the latter, the first steps of development may be observed at its anterior end, and on its upper surface, and even in the tracts of embryonic tissue that lie between the lobules, at a time when the development as a whole is well advanced. Now it is at those tardier points, at the anterior end and on the upper surface, that the first appearance of mammary secreting structure must be looked for. In the cat it has not been found practicable to trace the formation of the mammary acini from the embryonic tissue of the upper surface of the fat-body. If it is necessary to carry out the alleged parallelism in the same animal, it must suffice to state the hypothesis that in the cat the mammary acini begin where the fat ends, and that the latest differentiation of the embryonic cells in the fat-region is appropriated to a still more particular purpose, that is, to become the secreting structure of a gland. But at this point the field of observation must be changed from the cat to the guinea-pig.

It has been already explained that, whereas in the cat the lower end of the mammary gland lies altogether above the fat-body, or rather above the cushion of fat into which the latter is changed; in the guinea-pig, on the other hand, the mamma and the fat-tissue are interlocked on all sides, and the mamma is limited to the inguinal region. Whatever these differences may signify from the point of view of phylogeny or evolution, they at least make the guinea-pig a more convenient animal on which to demonstrate the present theory of mammary development by microscopic preparations. The fat-lobules of the mammary region in the guinea-pig do not form a fat-body; they never pass through the remarkable gland-like phase that the fat-body of the kitten is so well adapted to illustrate. But, on the other hand, the mammary development takes place

in the midst of the fat-development, and it is therefore easier to show that the matrix-tissue of the two kinds of structure is the same. The mere contiguity does not of course afford any proof, but it greatly simplifies the statement of the problem and the presentation of evidence. For the same reason as in the guinea-pig, the udder of the fœtal calf would probably be found very useful for putting this question to the proof. In a fœtal cow-calf, about half-grown, the udder is found to have its proper shape and its relative size, being a conical eminence completely raised above the skin, upwards of an inch in diameter at its base, and somewhat less in height. Two pairs of teats are also perfectly developed, and the rudiments of large ducts are found over a small space directly beneath the teats. The substance of the udder is a gelatinous mass, in the midst of which lie a large number of small round bodies of a somewhat different texture, like tubercles in the substance of an organ. These round tubercle-like bodies are distributed throughout the whole substance of the udder quite regularly, and it might be supposed that they were the already developed lobules of the gland, visible through the gelatinous stroma. On examination, however, they are found to be collections of fat-cells, developing from the gelatinous embryonic tissue of the udder at many regularly distributed centres. The abundant gelatinous tissue in which they occur is of the embryonic kind usual in the mesoblast, containing numerous spindle-cells and a large amount of hyaline intercellular substance. The hypothesis, as regards this form of udder, would be that the acini develope throughout the whole udder from the remaining embryonic tissue, in much the same way, and from much the same number of independent centres, as the fat-lobules had done before them. It was not possible, however, to put the hypothesis to the test, from want of suitable material.

In describing the development of the mamma in the guinea-pig, it is convenient at first to disregard the development of the ducts, and to treat the acini developing as if the ducts were non-existent. In Fig. 2 is shown a portion of a duct and terminal branches. The tissue surrounding it is a part of the embryonic tissue, of which the whole wedge-shaped body in the groin at one time consisted. The ducts now penetrate

the centre of it, and the fat-tissue lies immediately outside it. Those surviving tracts of embryonic tissue are seen to contain groups of cells at various points, which, at first sight, resemble the aggregates of embryonic cells from which the fat-lobule had developed. Turning now to Fig. 1, showing the state of the mamma about three weeks later, the place of the embryonic tissue round the duct is found to be taken by a large collection of acini, completely overshadowing the central duct, to which they are related. The rudimentary or potential lobule of the earlier period has expanded into a voluminous group of acini, each of which is much more like a small collection of fat-cells than the epithelium-covered recess of a secreting gland. The acini are essentially collections of fat-cells which have developed from the remaining tracts of the matrix-tissue by the side of the ducts, and which have undergone exactly the same process of transformation in the individual cell that the fat-tissue had undergone at an earlier period. The original wedge of embryonic tissue in the inguinal region has become fat-tissue, except along certain central tracts or planes in which the already-formed ducts lie; the ducts, and the embryonic tissue, among which they lie, form, as it were, an island of the original matrix that has escaped becoming fat-tissue. At a later stage of development, the encroachment of the fat is still greater, and the embryonic tissue remains only as narrow strips along the sides of the ducts and round their terminations. It is from these narrow margins of the original matrix that the acini develope. The great expansion of acini shown in Fig. 1 implies a very considerable development from so narrow a basis; but the process of expansion becomes intelligible by observing the mode of development of the acini singly. It is here that the observations now to be recorded agree with the general conclusions on gland-development arrived at by Goodsir.

If, in new-born guinea-pigs, the margins of embryonic tissue which run along the sides of the ducts, or extend from the ends of them in narrow planes through the fat, be examined closely, there will be frequently seen the appearances drawn in Fig. 4, *A*, *B*, and *C*, under a magnifying power of about 600 diameters. There is first distinguished a small cluster of

cells, as in *A*; one of the cells is vacuolated and has a large nucleus on the periphery, two other cells have a conical extension of protoplasm, and there is on the other side an elongated nuclear cell. In the margin of tissue by the side of the duct, these four cells are a distinct and isolated cluster. This margin of tissue can be seen, by careful examination, to contain many such, and among them groups of the kind shown in *B*. This group is more obviously an independent cluster or colony; the outer row of cells have an elongated crescentic form, and some of them have processes which appear to complete the circuit and retain the whole within a definite boundary. In *C* a similar appearance is shown; the cellular development is found in the midst of one of the narrow strips of embryonic tissue that extend from the duct through the fat. At the lowest part of the figure is a cluster of very minute nuclear cells; above them are two other rudimentary acini with better-marked characters. The lower of the two contains two large vacuolated cells, not distinguishable from fat-cells; these clusters are, however, quite certainly acini. It appears probable that the regular spherical arrangement of the cells forming an acinus is produced by means of the extensive vacuolation of one or more of the cells. The periphery of the vacuolated cells becomes the circular boundary of the acinus. If the figures *B* and *C* are compared, the crescentic cells in *B* that form the boundary of the acinus will be found to correspond to the peripheral nuclei of the large vacuolated cells in *C*. All the cells of the cluster, more or less, undergo the vacuolation at one time or another; the earliest vacuolations seem to determine the form and expansion of the acinus, and in the acini of Fig. 1 the process is seen to be quite general. These appearances, apart from their bearing on the homology with the fat-lobules, seem to point to a less rigid law of acinous development than that laid down by Goodsir. According to Goodsir, "an acinus is at first a single nucleated cell. From the nucleus of this cell others are produced. From these, again, others arise in the same manner. The parent cell, however, does not dissolve away, but remains as a covering to the whole mass, and is appended to the extremity of the duct. Its cavity, therefore, as a consequence of its mode of development, has no

communication with the duct." According to this view, based chiefly on studies of invertebrate or lower vertebrate animals, the boundary of the acinus is formed by the distended wall of a single cell, in the parent cavity of which all the cells of the acinus, or the future epithelium, have developed. However that may be, the present description agrees with that of Goodsir in the important point that the development of acini is not by means of protrusions of the ducts so as to form infundibula or recesses at many points along their course, but that it is an *interstitial development* from the embryonic tissue that surrounds the ducts. Those margins of embryonic tissue, it has been said, become extremely narrow by the time that the system of ducts and the surrounding fat are completely developed; so much so, that at some places they might be maintained to be nothing more, in relation to the ducts, than a submucous row of cells. Here again there is a striking agreement with the observations of Goodsir, and it will be seen from the quotation that he did not find the circumstance just mentioned to be inconsistent with the notion of interstitial development. The observation of Goodsir does not refer to the embryonic development, but to those periodical "developments" of glands from season to season, which he compared to their embryonic development. The example chosen is the testicle of a shark (*Squalus cornubicus*) in its various stages as it advanced from the resting state to the active secretory state at the time of sexual vigour. The acini "developed" as follows:

"1st. A single nucleated cell attached to the side of the duct, and protruding, as it were, its outer membrane.

"2nd. A cell containing a few young cells grouped in a mass within it; the parent cell presenting itself more prominently on the side of the duct.

"3rd. A cell attached by a pedicle to the duct, the pedicle being tubular and communicating with the duct; the cell itself being pyriform, but closed and full of nucleated cells.

"4th. Cells larger than the last, assuming more of a globular form, still closed, full of nucleated cells, and situated more towards the surface of the lobe.

"5th. The full-sized vesicles already described as situated at the surface of the lobe. These vesicles are spherical, per-

fectly closed; that part of the wall of each which is attached to the hollow pedicle forms a diaphragm across the passage, so that the vesicle has no communication with the ducts of the gland." When the contents of the acini are mature, the above-mentioned diaphragm, says Goodsir, is broken through, and the contents of the acini are discharged into the ducts.

Having described in the guinea-pig the mode of origin of the acini by the side of the ducts, and their appearance in a fully-expanded lobule at the time of birth, it will now be possible to trace the parallelism with the fat-development at all points. The cluster of four cells in Fig. 4 *A* (mamma of guinea-pig) is in every respect the same as those small groups of cells that indicate the beginning of a fat-lobule in the extreme inguinal region of the fœtal kitten; the presence of one or more vacuolated cells, around which the others are grouped, is no less characteristic of the latter than of the former, and this initial similarity is as striking as the resemblance at more mature periods. In the case of the kitten, these "germinal spots" of the matrix proceed to form the lobules of a fat-body, which has many points of resemblance to a gland; in the case of the guinea-pig they arise by the side of a system of ducts *already there*, and instead of forming a gland-like fat-body, they become the serviceable acini of a racemose gland. The stages A, B, and C of Fig. 3 (fat-lobule of kitten) may be compared to *A*, *B*, and *C* of Fig. 4 (mammary acinus of guinea-pig); while the expanded mammary lobule of Fig. 1 may be compared to a cluster of fat-lobules of the same gland, as they existed three weeks earlier. There is thus an identity as regards the matrix tissue, a similarity in the initial grouping of the embryonic cells, and a more than ordinarily striking similarity in the destiny or subsequent transformations of the cells. That destiny is that they become spherical, assuming a protoplasmic investment round the nucleus, and that they undergo a process of vacuolation. The two distinguishing features of the groups of cells that become the mammary acini are, (1) that they are the last of the embryonic cells to undergo their peculiar development, and (2) that they are ranged along the sides of ducts. In those two circumstances lies the differentiation of the mammary acini from the other parts of the fat-body or of the

inguinal fat-region. The comparative anatomy of the breast will throw some light on the way in which the differentiation has come about. It will be convenient to introduce this subject at once, in treating of the next section of the inquiry, viz. the development of the ducts.

In the guinea-pig a system of ducts is found extending throughout the entire region of the future gland several weeks before any acini can be distinguished as such, and both in the fœtal kitten and guinea-pig the nipples are well formed at a still earlier period. This order of development in the individual rodent or carnivorous animal is a remarkable reversal of the order of appearance of the various structures in the phylogenetic succession of mammalian animals. In the *Ornithorhynchus* and *Echidna* there is no nipple, and there are, strictly speaking, no ducts. The mamma is composed of about 100—200 flask-shaped follicles, each of which terminates in the skin by an elongated neck. The necks into which the follicles are drawn out, and by which they are attached to the skin, may be regarded as an incipient system of ducts. In each follicle there does not appear to be more than a single central passage. The gland, in fact, belongs to the follicular order of glands, which appear to be the primitive type of secreting structures, and which often occur in the invertebrata where vertebrate animals have glands of the acinous type. The follicles are generally elongated, the blind extremity being slightly pointed. The substance of the follicle is a mass of secreting cells, in whose midst a more or less regular passage exists near its attached end, by means of which the secretion is poured out. The mammary follicles of the *Echidna* are somewhat more complex than this, but the plan of them is essentially the same. It has, indeed, been asserted by Owen[1] that the structure of the gland in the *Echidna* is "on the same general plan as that of the mammary glands in higher mammals," and he states, in particular, that the duct by which the follicle opens on the skin is "directly continued from a canal which may be traced about half way toward the fundus of the lobule; the canal gives off numerous short branches from its circumference, which subdivide and terminate in clusters of sub-spherical 'acini' or

[1] *Philosoph'cal Transactions*, 1875.

secerning cellules." He also states that the structure closely resembles that of the *Ornithorhynchus*. Through the kindness of Professor Flower I have been able to examine the glands of both animals with the microscope. That of the *Echidna* was in its most fully developed state, while that of the *Ornithorhynchus* was in an extremely "involuted" condition, and was not one-tenth the volume of the other. In a former investigation I described at great length the histological nature of those periodical processes of "evolution" and "involution," and among other noticeable points was this, that in the full development of the secreting structure during lactation it was difficult to see the system of ducts on account of the great expansion of the acini which concealed them, while in the shrunken or involuted state of the gland, when the function was in abeyance, the ducts and clusters of terminal acini were everywhere prominent, and their branching arrangement could be clearly traced. So that, if the microscopic examination revealed no system of ducts and terminal acini in the expanded gland of the *Echidna,* they ought at least to have been quite visible in the involuted gland of the *Ornithorhynchus*. But such was not the case. A single central passage ran through each lobule, and it is probable that it had, when fresh, a lining of columnar epithelium; but a racemose system of ducts and acini was certainly not present; and I can only explain Professor Owen's statement by supposing that the injection which he used must have penetrated through the substance of the follicle along certain regular lines where the resistance was less. The minute structure of the mamma in those two animals will be briefly referred to afterwards; for the present they may be safely considered to be glands of the follicular type. The class of animals that come next to the *Monotremata,* as regards the complexity of the breasts, are the *Cetacea;* the marsupial animals in this respect must be considered somewhat higher. In the porpoise each gland has a single common duct, which runs from the nipple downwards to a considerable depth. Around this central vertical duct the secreting follicles of the gland are grouped in more or less horizontal planes at various depths. The structure is still essentially follicular, but the follicles, instead of opening on the skin each by its own duct, discharge into a common conduit at

various points. It can easily be shown diagrammatically how the racemose system of ducts is produced by extending the same principle of centralisation, of which the beginning is seen in the cetacean mamma. With the system of ducts comes necessarily a subdivision of the parenchyma into acini. It is perhaps impossible now to trace, in nature, all the steps by which this modification came about, but it appears certain that the original part of the mamma was its parenchyma, or the solid aggregates of its secreting cells, and that the ducts, which greatly help to economise the secretion, were acquired later. Now, as regards this particular organ of the body, the principle that the embryonic development in the individual is a brief recapitulation, in their order, of all the acquisitions that have been made in the phylogenetic succession, does not hold good. The nipple is the latest addition or improvement on the original mamma, but in the guinea-pig and cat it is developed in the skin long before the secreting structure is developed in the lower stratum. The elaborate system of ducts constitutes the other addition or improvement, but in the guinea-pig the plan of them is completely laid down throughout the whole extent of the future gland, before the essential secreting structure or parenchyma makes its appearance as such. The early appearance of the ducts has been noticed by the writers on the development of the breast, and it is no doubt owing to the circumstance of the ducts appearing first in the individual, growing, as it were, from the rete mucosum downwards, that the gland has been taken to be essentially a complex reduplication of the ectoderm, the recesses or infundibula of which were utilised for secretion. It has been pointed out, at the beginning of this paper, that the theory has been accepted without due consideration of the evidence, or rather want of evidence, on which it was based, and in the subsequent parts of the paper another account of the development has been given, resting mainly on histological evidence, but supported also by the considerations adduced above from comparative anatomy.

But the question then remains, How comes it that this alleged order of acquisition of the various parts of the mamma in the evolution of animals, is reversed in the development of the organ in an individual of the higher mammalians, such as

the guinea-pig? In answering this question it will be necessary to make use of an argument that is stated with great clearness in Mr Herbert Spencer's "Principles of Biology," and which appears to be an original generalisation of that writer. The following extract[1] will present this argument in the briefest possible way.

"The same kind of structure is not always produced in the same ways; and some allied groups of organisms have modes of evolution which appear to be radically contrasted. The two modes are broadly distinguishable as the *direct* and the *indirect*. They may severally characterise the general course of evolution as a whole, and the course of evolution in particular organs.... Thus in the immense majority of articulate animals, metamorphoses, more or less marked and more or less numerous, are passed through on the way to maturity. The familiar transformations of insects show us how circuitous is the route by which the embryo-form arrives at the adult form among some divisions of the *Articulata*. But there are other divisions, as the lower *Arachnida*, in which the unfolding of the egg into the adult takes place in the simplest manner: the substance grows towards its appointed shape by the shortest route."

The general rule is that the indirect development characterises the most highly organised forms; conversely it is direct in a large proportion of the lower types. One of Mr Spencer's illustrations from social affairs is so admirable that no excuse is needed for occupying space with it here.

"A new town in the United States arises not at all after the old method of gradual accumulations round a nucleus, and successive small modifications of structure accompanying increase of size; but it grows up over a large area according to a predetermined plan; and there are developed, at the outset, those various civil, ecclesiastical and industrial centres, which the incipient city will require."

The argument proceeds as follows:

"Now on the hypothesis of evolution, all organs must have been originally formed upon the indirect method, by the accumulation of modifications upon modifications; and if the development of the embryo repeats the development of ancestral races,

[1] *Principles of Biology*, Vol. I. p. 371 et seq.

organs must be thus formed in the embryo. To a considerable extent they are thus formed."

Mr Spencer then gives examples of organs that are formed according to the indirect mode, and of other organs formed according to the direct, and concludes that, on the hypothesis of evolution, the direct mode of development in the latter class must have been substituted for the indirect.

The bearing of this speculation on the development of the mamma and its various parts, will now become apparent. As there are certain classes of animals distinguished from other classes by the "directness" of their development, and as there are some organs so distinguished from other organs in the same animal, so there are, in one and the same organ, some parts developed "directly" and other parts developed "indirectly." In the mammary gland, the nipple and ducts are developed directly, and the secreting structure, or the acini, are developed indirectly. In a mammary gland, the ducts were originally spaces formed in the midst of the parenchyma by a modification or adaptation of the same along certain central tracts. But the developing gland in the individual (guinea-pig, for example) does not repeat the particular steps of adaptation or modification, inasmuch as the ducts are laid down throughout their whole extent before the secreting structure appears. The indirect process of adaptation is replaced by a direct mode of origin. It will now be suitable to introduce the facts relating to the origin of the ducts.

In the wedge-shaped body of embryonic tissue in the groin of a fœtal guinea-pig less than half grown, but with nipple already formed, there are seen, extending backwards from the nipple, certain narrow tracts of cells, which are simply the embryonic cells of the part closely packed together. These tracts of closely-packed cells form at various points throughout the embryonic mass independently of each other, and no continuous extension of them can be traced from the nipple. At this period of development, the fat-lobules are beginning to form from the same matrix, and it is impossible in some cases to distinguish the elongated and narrow collections of rudimentary fat-cells from the first-mentioned linear aggregations of cells. But there are some unambiguous cases in which a dis-

tinct lumen can be seen in the narrow tract of cells, both in the longitudinal and in the cross section, and it can hardly be doubted that these are rudimentary ducts. The appearances observed in the udder of the fœtal calf, and in the mammary region of the new-born rat, also favour this view of the origin of the ducts. There is certainly no evidence of a process of growth downwards from the rete mucosum of the nipple. The mode in which a communication is formed between the epidermic excavation or depression in the nipple, and the ducts forming in the lower stratum, does not seem to present any great difficulty of explanation; but it has been found necessary, for other reasons, to omit it from the present paper.

The ducts are therefore held to be formed as aggregations of the embryonic cells of the matrix along certain predetermined lines; that elementary fact seems to be established, and it matters little for the present purpose that no circumstantial account can be given of the manner in which these cord-like structures are formed into hollow tubes lined, in the mature state, with columnar epithelium. Certain facts of a negative kind can however be made out. In the course of formation of the ducts, the embryonic cells do not appear to undergo any of the very marked transformations that have been described for the fat-lobules and the cells of the acini. As compared with those other structures that the matrix-tissue gives origin to, the ducts may be said to be formed out of the embryonic cells by the "direct" mode. In Mr Spencer's words, "the substance grows towards its appointed shape by the shortest route." It is this shortened or direct mode of development that must be held to explain the early appearance of the ducts. But the question still remains, how it is that in the case of the ducts their development is by the direct, and not by the indirect mode. This brings us back to Mr Spencer's question: "How comes the direct mode of development to have been substituted for the indirect?" It will here be necessary to resume the quotation from Mr Spencer.

"Supposing it were possible for a race of organisms to have continued propagating itself through an indefinitely long period without any change of conditions necessitating change of structure; there would be reached so complete a congruity between the organic aggregate and its physiological units, that the units

would arrange themselves directly into a structure like that of the adult organism: the germ would put on the proper characters of the species with little or no transposition of substance. But in the absence of any such constancy of conditions and structure, what may we expect? We may expect that where the conditions and structure have been most constant, the mode of development will be the most direct; and that it will be the most indirect where there have been the greatest and most numerous changes in the habits and structures of ancestral races of organisms....Between different parts in the same embryo, there are unlikenesses in the method of formation, which seem to have kindred meanings."

The former part of Mr Spencer's argument was made to apply to different parts of the same organ, and it will now be seen how the reasoning of the last quotation applies to the different modes of development within the mamma.

Comparing the parts of the mature mamma with one another, the ducts are those parts that exist throughout the life of the individual "without any change of conditions necessitating change of structure;" whereas the secretory activity of the gland depends on constant changes in the cells of the acini. This fact cannot be better illustrated than by reference to the periodical processes of "involution" and "evolution" to which the mamma is liable. In those processes the ducts alone continue as they were during the state of active lactation; the whole processes of upfolding and unfolding take place in the acini or true secreting parts of the gland. The ducts play a purely mechanical part, and they remain unchanged from the time that their development was completed throughout the whole lifetime of the animal. According to Mr Spencer's argument as extended, it is under such circumstances as these that the direct mode of development is substituted for the indirect; and it would appear to be in accordance with this principle that the ducts of the mamma, though they are additions to the primitive mamma and acquired comparatively late in the succession of mammalian animals, are in the individual higher mammalian developed from the matrix-tissue of the gland before the secreting structure itself. To borrow Mr Spencer's illustration of a new town in the United States, the ducts of the breast are like

the roads that are laid down before any houses are built by the side of them. In the primitive state of a community, however, dwellings were first erected, and afterwards paths were struck out between them; and in the primitive condition of the breast, the secreting follicles of the gland existed first, and these were gradually connected together by a system of ducts.

The conclusions of the first part of this inquiry are:

(1) That the mammary acini of the guinea-pig develope at many separate points in a matrix-tissue; that the embryonic cells, from which they develope, are of the same kind that give origin to the surrounding fat-tissue; and that the process of development of the mammary acini is step for step the same as that of the fat-lobules.

(2) That the ducts of the mamma develope from the same matrix-tissue by direct aggregation of the embryonic cells along predetermined lines; that the ducts develope in the individual guinea-pig before the acini, whereas in the phylogenetic succession the ducts are a later acquisition; and that this reversal of the order of acquisition of parts is in accordance with the principle stated by Mr Herbert Spencer that, under certain circumstances, the *direct* mode of development tends to be substituted for the *indirect*.

Having thus far described the mode of development of the mammary structure, it remains to treat of the development of the mammary function. The development of the function, in the largest sense of the term, means the acquisition of the mamma as a mammalian characteristic, and this important matter cannot be gone into until the question of the homology of the mamma has been discussed. The homology of the mamma is a subject large enough for a separate inquiry; but there are certain obvious inferences from the foregoing histological facts, and certain elementary facts in the comparative anatomy, which may be summarily stated here.

The homologue of the mamma is not a cutaneous gland, or, at any rate, it is not a recess of the ectoderm; but it is a fat-body. The homology of the mamma is thus placed on a much wider basis. The mammary glands of the *Ornithorhynchus* and *Echidna* may be regarded with equal justice as

secreting glands or as fat-bodies. From the observations of Mr G. Bennett[1], made in Australia, there can be no doubt that the gland of the duck-bill does secrete a milky fluid at a particular season, although the information on this subject is by no means full. Thus, with respect to a particular case, Mr Bennett writes: "This female had evidently just produced her young...The mammary glands on each side were very large; but it is a curious and rather an interesting circumstance in the œconomy of this animal, that after having been shot, no milk could be expressed from the glands. This was the more surprising to me, as the glands were very vascular on the surface, the mammary artery ramifying over them in a most beautiful and distinct manner. The fur still covered that portion of the integument on which the ducts terminated, and there was no appearance of a projecting nipple." But, in other cases, Mr Bennett has "seen the milk exuding from the ducts upon the integument." The full expansion of the organ is found only in the animals shot about the month of December, which appears to be the season of fertility; specimens shot in August had the gland in a greatly contracted state, and in most of the specimens that reach this country the gland is in its extreme "involuted" condition, and so small as almost to escape notice. In that condition of the gland the follicles are small oat-shaped bodies of a brown colour, arranged in the form of a fan and connected to the skin by somewhat elongated solid necks less than a line thick. The area of skin to which the follicles converge is about half an inch long and about an eighth broad. When the hair is scraped clean from this surface of skin, not a single trace of pores or orifices of the ducts can be discovered, even with a magnifying glass; and it is probable that the openings by which the secretion exudes are not permanent passages, but called into existence only when the gland is in its active state. The gland might therefore be compared to one of those fat-bodies that undergo expansion from season to season, with this difference, that the fluid contents of the cells find their way out of the follicles and through the skin when the expansion or the internal pressure is at its height. Another curious point of resemblance to

[1] *Transactions of Zool. Society*, Vol. I. p. 251.

the fat-bodies is as follows. The brown colour of the shrunken follicles in the *Ornithorhynchus* depends on the presence of brown pigment in the individual cells. Each follicle is divided into a large number of somewhat rectangular or lozenge-shaped compartments, and each of these small spaces contains several round granular cells filled with brown pigment. The necks of the shrunken follicles are filled also with the brown pigmented cells. When these follicles expand, the compartments have become very much larger, and they contain, not a few granular pigmented cells, but an immense number of vesiculated cells occupying the entire space, or coming into view at various depths, and packed together in the same way as the cells of fat-tissue are packed. These vesicles are not all of the same size; most of them are much smaller than the ordinary fat-cells, but some of them are almost as large. This appearance can be seen in the expanded gland of the *Echidna*. Now these differences between the resting state and the active state of the gland are precisely the differences, as regards the individual cell, between the fat-bodies in their winter condition and in their spring or sexual condition. The cells of the winter fat-body, or the so-called atrophied fat-cells, are also found, in some cases at least, as round granular cells containing a brownish pigment, whereas the greatly expanded fat-body consists of lobules of ordinary fat-tissue.

Another direction in which the homology may be pursued is the following. The mammary gland is found only in the female *Ornithorhynchus* and *Echidna*. But the males of the *Ornithorhynchus* and *Echidna* have also a gland peculiar to them, which resembles the mamma in being a sexual gland, and in being subject to periods of expansion and functional activity from season to season. This gland is the *glandula femoralis*, situated on each side on the back of the thigh, and discharging by a long duct which runs down the leg and opens on the plantar aspect at the "spur." There is a certain probability of this gland being the homologue of the female gland, and when the very singular differences between the mammæ in the male and female cetaceans are observed, this probability becomes much stronger. I am indebted to Professor Flower for pointing out to me the peculiarity of the

mamma in the male porpoise, as shown in preparations made by himself. Instead of there being a pair of ducts, one on each side, as in the female, there is only one duct which opens by a round pore without a nipple in the middle line of the body at a point much farther back than in the female. Now, by those two circumstances, the singleness of the duct and its caudal position, the mamma of the male porpoise is brought within reach of comparison with the femoral gland of the male duck-bill. This is nothing more than a curious suggestion; but if the porpoise be represented with a pair of hind-limbs, the single duct of the male mamma opening in the middle line far back on the ventral surface would then be represented by a pair of ducts going with the limbs, and that is exactly the condition in the male duck-bill.

The *glandula femoralis* of the male animal is a gland of more complex structure than the mamma of the female, not only as regards its duct but also as regards its parenchyma; it is higher than the female gland in much the same degree that the cetacean mamma is higher than the mamma of the monotremes. The speculation that follows is to be taken for what it is worth. If the *glandula femoralis* is the homologue of the mamma, it is at the same time a "higher" gland; and, according to modern ideas, it may be said to have been acquired earlier. It therefore follows that the mamma was first acquired by the male. Now that conclusion would bring the mamma within the Darwinian class of "secondary sexual characters" acquired by sexual selection. Mr Darwin, indeed, has excluded the mamma from that category, but it is impossible to avoid thinking that Mr Darwin's reasons for this exemption are somewhat arbitrary[1]. As a secondary sexual character, first acquired by the male, the mamma would be classed with the accessory sexual structures, such as the scent glands. In this way, the conflicting opinions that arose in 1826, when the mamma of the female *Ornithorhynchus* was first described by J. F. Meckel, would be reconciled. Meckel's view, that the gland was a true mammary gland, was opposed by Geoffroy St Hilaire, who, from an independent examination of it, strongly insisted on its follicular type, and concluded that the gland was "analogous

[1] *The Descent of Man, and Selection in Relation to Sex*, Vol. I. 254 and 256.

rather to those glands for the secretion of a lubricating fluid, that are disposed along the flanks of the aquatic reptiles and fishes, or to the odoriferous follicles of quadrupeds, and especially to those which are found on the sides of the abdomen in shrews[1]." Setting aside entirely the question of analogy, as relating to function, it may be reasonably contended that the view of Geoffroy St Hilaire is correct as a view of homology; and facts might be adduced to show that such a view of the homology would not prejudice the doctrine of homology already followed out along an independent line, viz. that the homologue of the mamma is a fat-body.

Apart from such considerations on the homology of the mamma, which are put forward purely as speculations without the necessary support of details, there is an aspect of the development of the mammary function which can be conveniently discussed in connexion with the histological details of the first part of the paper.

In a previous investigation[2] on the physiological processes of the mamma, I showed that the gland, in its periodical preparation, or "evolution" during each pregnancy, was continuing all the time to perform its function in an imperfect degree, and that the well-marked law of cell-formation, or cell-transformation, that obtained during the imperfect state of the gland's activity, was also the cellular law of the function when the lactation was at its height. What those cellular changes are, will be found described in great detail in the paper referred to. Now the developmental changes in the embryo, which have been described, are, for the individual cell, exactly the same as the series of changes during each periodical "evolution." The regularly recurring periods of sexual excitement of the mamma are regular repetitions of its developmental process, and the function of the mamma may be said to be a sustained repetition of its development. The milk of the new-born guinea-pig is a developmental product, derived from the cells of the acini when they have reached the highest point of their development. The vacuolated or fat-

[1] These statements are made in a letter published in the *Annales des Sciences Naturelles*, IX. 457. I have not been able to find a more complete statement of M. Geoffroy's views.

[2] *Loc. cit.*

like cells shown in Fig. 1 burst their vacuoles and discharge the fluid, while the nuclei of the cells remain over as the future epithelium. After this discharge of developmental milk is over, the acini contract their circuit very much, and in the primiparous guinea-pig, at the beginning of pregnancy, they are found as small round spaces containing a few nuclear cells. As the pregnancy advances, the "evolution" of the now mature gland proceeds. This process I have already minutely described elsewhere, and it must suffice to mention here that the end of the process again finds the acini of the gland enlarged and occupied with vacuolated cells. The vacuolation process of the epithelium is the process by which the milk is formed all through the lactation period. The lactation is a continuance of the periodical sexual excitement of the gland at its highest point. The secretory process is thus parallel with the developmental process. If secretion were an end in itself, that parallelism might not signify much. But the development is the ultimate fact; and it is so far an explanation of the secretion to find that it consists in a repetition of those cellular changes which the cells of the part went through in their development.

EXPLANATION OF PLATE.

Fig. 1. Section from the mamma of a guinea-pig four days old. A rounded or pyriform lobule made up of a large number of acini the cavities of which are distended with vacuolated cells. Nuclei are to be seen among the vacuolated cells at various depths. × 300.

Fig. 2. Section from the mamma of a fœtal guinea pig about three weeks before birth. System of ducts surrounded by embryonic tissue. × 300.

Fig. 3. A. From the gelatinous tissue in the inguinal region of a fœtal kitten 2½ inches long. In the middle of the figure a small group of the embryonic cells undergoing changes to become fat-cells. × 300.

B. From the gland-like tissue in the same region of a fœtal kitten 3½ inches long. Later stage of the fat-lobule. × 300.

C. From the fully developed fat-body in the inguinal region of a new-born kitten. A small lobule of the fat-body, showing the vacuolated condition of the cells. × 300.

Fig. 4. From the mammæ of new-born guinea pigs. × about 600.

A. Group of four cells in the embryonic tissue at the side of a duct. The earliest appearance of an acinus.

B. Similar group showing a later stage of the acinus.

C. The upper part of the figure shows two acini developing in the midst of a tract of embryonic tissue. Several of the cells extensively vacuolated.

SOME GENERAL OBSERVATIONS ON THE PLACENTA, WITH ESPECIAL REFERENCE TO THE THEORY OF EVOLUTION. By PROFESSOR TURNER.

(The following observations formed the conclusion of my 2nd series of Lectures "On the Comparative Anatomy of the Placenta," delivered in June, 1876, in the Theatre of the Royal College of Surgeons of England.)

FROM the description which I have now given of the diffused, the polycotyledonary, the zonary[1], the dome-shaped and the discoid forms of placenta, we are in a position to pass briefly in review the structure of the principal examples, with the view of ascertaining if the organ presents different types of structure in different mammals, or if the entire series of placentæ are constructed on such a uniform plan as would justify one in conceiving that the several structural modifications could have been evolved out of a simple fundamental form.

At the outset we may state that the presence of certain structures seems to be necessary for the performance of the functions of a placenta, and the most simple arrangement of these structures would constitute a placenta in its most generalized form. The fundamental condition of the fœtal part of the placenta would be a smooth plane-surfaced vascular membrane, covered by a layer of pavement epithelium. The fundamental condition of the maternal placenta would be a smooth plane-surfaced vascular membrane covered by a layer of columnar epithelium. The two membranes would be parallel to and in apposition with each other, the fœtal epithelium being in

[1] See this *Journal*, Oct. 1875, for an account of the diffused, polycotyledonary and zonary placentæ; also, and more in detail, my published *Lectures on the Comparative Anatomy of the Placenta*, 1st series, Edinburgh, 1876. I described the dome-shaped placenta of the Sloth in *Trans. Roy. Soc. Edinburgh*, 1873; but the detailed account of the discoid placenta has not yet been printed. I have not thought it necessary in this place to enter into the question of the relation of the utricular glands to the uterine crypts, and to the chorion, as I have, in my 1st series of Lectures, expressed my opinion on this matter.

contact with the maternal epithelium, so that the fœtal capillaries would be separated from the maternal capillaries by the two apposed layers of epithelium. This arrangement would occupy the whole of the surface of the chorion for the fœtal placenta, and the whole of the uterine mucous membrane for the maternal placenta (fig. 1).

The diffused placenta of the common Pig presents the least departure from this generalized form. The evidence of specialization consists in the formation of ridges and short simple villi on the surface of the fœtal chorion, and the coincident production of shallow simple depressions or crypts in the uterine mucous membrane. The two epithelia preserve their fundamental form and relative position, and the fœtal and maternal vessels continue of the size of ordinary capillaries. In this animal the villi and crypts are not diffused over the whole of the chorion and uterine mucous membrane; the polar portions of which are smooth, but preserve their vascularity (fig. 2).

In the diffused placenta of the Mare, the *Cetacea*, and the Lemurs, a somewhat more complicated, and more highly specialized arrangement exists. The short villi of the chorion give origin to simple microscopic offshoots, and the uterine crypts are divided into minute compartments for their reception, so that each villous tuft, with the corresponding depression in the mucosa, forms a microscopic cotyledon. The two sets of vessels preserve their capillary size, and the epithelia their relative positions; though the maternal epithelium may have undergone some modification in shape.

In the polycotyledonary placenta of the Ruminants, a still more specialized disposition exists. The villi are considerably elongated and give origin to numerous branches, and at the same time the uterine crypts are deepened into pits, from which shallow compartments proceed, for the reception of the long many-branched villi. From the aggregation of a number of these into definite masses the large cotyledons arise, which one is familiar with in the placenta of the Cow, Sheep, and other typical Ruminants. The fœtal and maternal vessels possess the size of ordinary capillaries, and the epithelia retain their fundamental relations to each other, though the maternal epithelium has not unfrequently lost its columnar form (fig. 3). The inter-

cotyledonary parts of the chorion and uterine mucosa, as is the case in most Ruminants, are smooth, though retaining their vascularity and epithelial covered surfaces; but in the Giraffe, not only are smaller cotyledons, sometimes not more than two lines in diameter, developed in the interspaces between the normal cotyledons, but short villi spring from the external surface of the chorion either singly, or in rows and clusters.

Another specialization is met with in the zonary placenta, in which the villi assume a sinuous form and give rise to broad lateral offshoots, or perhaps branch in an arborescent manner. In correlation with these modes of arrangement of the villi, the uterine mucosa assumes the form of complex sinuous folds, or it becomes divided into a microscopic trabecular frame-work, in the meshes of which the villi are lodged. The maternal epithelium may possess a well-marked columnar form as in the Seal and Fox; or it may be stunted and rectangular, as in the Cat; and the maternal vessels, instead of forming ordinary capillaries, may dilate into vessels two, three, or four times as large as the fœtal capillaries. In these placentæ the dilated maternal blood-vessels, invested by the maternal epithelium, lie amidst groups of villi (figs. 4, 5). Hence each maternal blood-vessel, with its epithelial investment, is in relation not to a single villus, as is the case in the diffused and polycotyledonary placentæ, but to the several villi which surround it. Although the subdivision of the maternal mucosa into trabeculæ causes it to lose the regular crypt-like arrangement of the diffused and polycotyledonary placentæ, yet the relative position of the several structures remains the same, and the fœtal and maternal blood-vessels are separated from each other by the layers of epithelium.

Another specialization is met with in the dome-shaped placenta of the Sloth, in which the maternal vessels are even more dilated than in the zonary placenta. They possess a serpentine course, and wind in and out between the villi. The maternal epithelium, which lies in close relation to the exterior of the maternal blood-vessel, is not columnar in form, but consists of polygonal flattened cells (fig. 6). The tortuous arrangement of the dilated vessels of the uterine mucosa obscures the crypt-like character of the depressions in which the villi are lodged, but

Fig. 1.

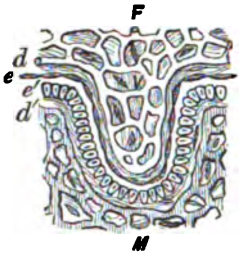


Fig. 2.

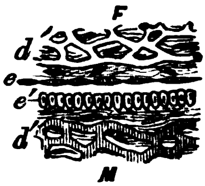


Fig. 3.

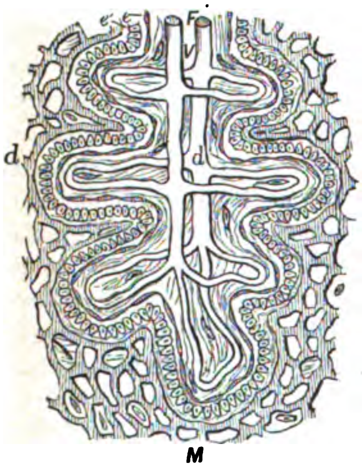
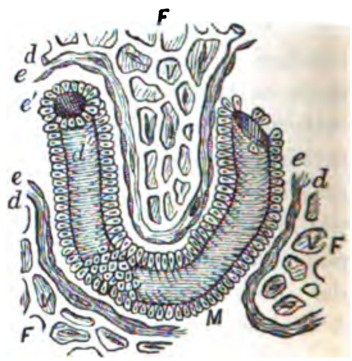


Fig. 4.



EXPLANATION OF FIGURES.

Throughout the series of diagrammatic representations of the minute structure of the Placenta the same letters have been used to indicate similar parts. *F* the fœtal, *M* the maternal placenta. *e* epithelium of chorion. *e'* epithelium of maternal placenta. *d* fœtal blood-vessels. *d'* maternal blood-vessels. *v* villus.

Fig. 1. Structure of placenta of a Pig.
Fig. 2. Placenta in its most generalized form.
Fig. 3. Structure of placenta of a Cow.
Fig. 4. Structure of placenta of a Fox.

Figs. 5, 6.

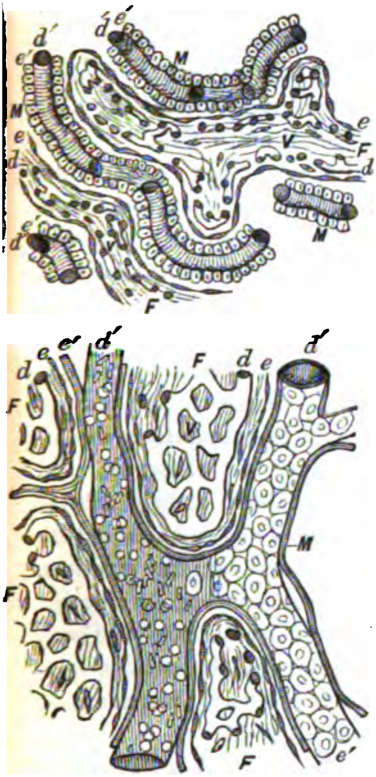


Fig. 7.

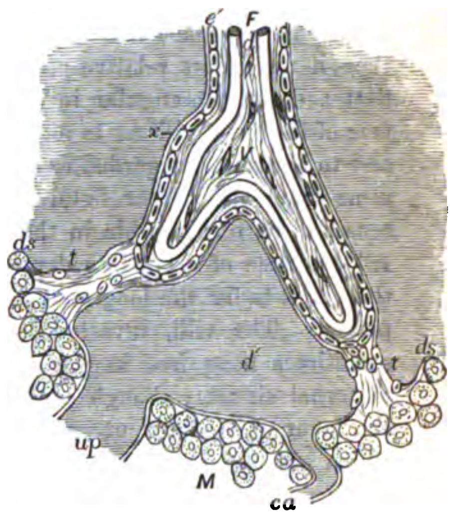


Fig. 5. Structure of placenta of a Cat.

Fig. 6. Structure of placenta of a Sloth. On the right side of the figure the flat maternal epithelial scales are shown *in situ*. On the left side they are removed, and the dilated maternal vessel with its blood-corpuscles is exposed.

Fig. 7. Structure of Human placenta. In addition to the letters already referred to, *ds*, *ds*, represent the decidua serotina of the placenta; *t*, *t* trabeculæ of serotina passing to the fœtal villi; *ca* curling artery; *up* utero-placental vein; *x* a prolongation of maternal tissue on the exterior of the villus outside the cellular layer *e′*, which may represent either the endothelium of the maternal blood-vessel, or delicate connective tissue belonging to the serotina, or both. The layer *e′* represents maternal cells derived from the serotina. The layer of fœtal epithelium cannot be seen on the villi of the fully formed human placenta.

The diagrams were drawn on wood by my assistant, Dr J. H. Scott.

the relative position of the constituent structures is the same as in other forms of placenta[1].

In the discoid Human placenta a more highly specialized arrangement exists. The maternal vessels in the substance of the placenta have not only lost their tubular cylindrical form, but have become expanded into a freely communicating series of irregular, cavernous, intra-placental sinuses, so that their derivation from the vessels of the non-gravid mucosa is, at the first sight, difficult to recognize. The maternal epithelium has also undergone a remarkable change in its shape and connections, though not in its relative position. It has become somewhat flattened and rectangular in shape, and so fused with the surface of the fœtal villi as to form a cellular investment for them, and to be usually regarded as a part of their structure. At the same time the proper fœtal epithelial covering of the villus ceases to be recognisable in the fully formed Human placenta. All evidence of crypt-like depressions in the maternal part of the placenta for the lodgment of the villi has completely disappeared. The villi, invested by the layer of maternal cells, sometimes hang free in the irregularly dilated intra-placental maternal sinuses; though at other times they are anchored to the layer of modified uterine mucosa, named *decidua serotina*, which walls in the placenta on the uterine aspect, by slender trabecular prolongations of the serotina. Notwithstanding these modifications in the structural arrangements, the relative position of the fœtal and maternal vascular systems is the same as in the least specialized forms of placenta (fig. 7).

The different varieties of the placenta met with in mammals

[1] When I wrote in 1878 (*Trans. Roy. Soc. Edinburgh*, 1878) my memoir on the Placentation of the Sloths, I had not then recognised the presence of a layer of cells situated between the dilated maternal blood-vessels and the villi of the chorion, and belonging to the uterine or maternal part of the placenta. The observations which I have since that time made on the placenta in various animals, more especially in the *Carnivora* and *Pinnipedia*, and the recognition in the mammalia generally of a layer of maternal epithelium interposed between the maternal blood-vessels and the chorion, have led me to re-investigate the Sloth's placenta with especial reference to this question. As the result of my enquiries I have found a layer of flattened, polygonal cells, in close apposition to each other by their margins, lying on the dilated maternal blood-vessels, and interposed between them and the villous chorion. These cells occupy therefore the same relative position as the columnar epithelium in the placenta of the Pig, Fox or Seal, but from the thinness of the layer do not so easily attract attention.

all possess the structural characters of the common or fundamental type-form, and may be conceived as having been evolved out of this simple type by slight modifications in arrangement. The process of evolution would be effected by the assumption of a greater extent of complexity in the foldings, on the one hand of the villous chorion, on the other hand of the uterine mucous membrane, with, in addition, in some placentæ, modifications in the relative size of the maternal blood-vessels and in the form of the maternal epithelial cells. The fœtal vessels always remain of ordinary capillary size, and the squamous epithelial covering of the villi may either persist, or become so obscured as the interlocking of the fœtal and maternal parts of the placenta progresses, that it cannot be recognised as a separate layer. The various forms of diffused placenta present the smallest amount of departure from the fundamental type, whilst the discoid human placenta is the most highly specialized.

It is to be observed that a correspondence in external form between different placentæ by no means indicates an exact accordance in the minute structure of their constituent parts. For whilst the discoid Human placenta has its intra-placental maternal vessels so modified that all trace of their original tubular, capillary form has completely disappeared, in the discoid placenta of the Rabbit and Guinea-pig they retain the capillary character, though in the part of the placenta which lies next the wall of the uterus they present a considerable extent of dilatation. Though the placenta in *Orycteropus* has, like the *Carnivora* and *Pinnipedia*, a zonary form, its fœtal and maternal portions may be so easily separated from each other, that it would seem to be referrible to the non-deciduate group of placentæ, and not, as is the case with the Seals and Carnivores, to the deciduata.

Throughout the whole series of placentæ there is interposed between the vascular chorion of the fœtus and the maternal blood-vessels—whether those blood-vessels be simple capillaries, dilated capillaries, or irregular cavernous spaces—a layer of cells, which is in close relation to the maternal blood-vessels. They constitute, or are derived from, the epithelium of the uterine mucous membrane, and belong to the maternal part of the placenta. They sometimes retain the fundamental columnar

form, but not unfrequently are modified in shape. This cell-layer is, I believe, a layer of secreting epithelium destined to elaborate material from the maternal blood for the nutrition of the fœtus.

But whilst the structure of the placenta in different mammals is so uniform in its main features, that the possibility of an evolution of the more complex from the more simple forms is quite conceivable, the anatomical structure does not favour the supposition that the evolution has gone on as a continuous process from the diffused, through the polycotyledonary, zonary and dome-shaped group-forms, until at length the highly specialized discoid placenta of Monkeys and of Man has been produced. There is indeed no difficulty in conceiving the evolution of a polycotyledonary placenta out of a diffused, through the atrophy of villi and crypts on some portions of the chorionic and uterine surfaces and their increased development on others, but the evidence is against the view, that the zonary has been evolved out of the polycotyledonary and the discoid out of the zonary. In the zonary placenta the villi and crypts, notwithstanding their specialized form, are yet diffused over the area of the placental girdle, whilst the poles are smooth. As smoothness of the poles of the chorion exists also to a greater or less degree in most examples of the diffused placenta, it would seem as if the evolution of the zonary had been directly from the diffused, through the occurrence of a more extensive atrophy, in the polar regions, in conjunction with certain specializations in the equatorial zone; and the placenta of *Orycteropus*[1] would appear to present a transition between the more characteristic examples of the diffused and zonary forms. That the discoid placenta has been evolved out of the zonary or the dome-shaped is also very improbable, for the latter group-forms exhibit in some features of structure a greater extent of specialization than the discoid placenta does in certain animals. Thus dilated maternal capillaries occur throughout the placenta in the Seals, Carnivores and Sloths, and form a more highly specialized condition of the vessels of the maternal placenta than exists in the discoid placenta of the Rabbit and Guinea-pig, in which the dilatation of the maternal vessels appears to be limited to the part of the

[1] This *Journal*, July, 1876, p. 693.

placenta which lies next the wall of the uterus, and not to be general throughout the entire organ. In some other features of structure, however, the placenta of the Rabbit or Guinea-pig is more highly specialized than is the zonary placenta. It seems to me therefore much more probable, if the several forms of placenta have been produced by a process of evolution, that they have arisen from some common fundamental form, the closest existing representative of which is the diffused placenta, rather than that the evolution has been in a continuous series through the various group-forms. This conclusion is supported by the well-known fact that in the highly specialized Human placenta the villi of the chorion in an early stage of development are diffused over the whole of its surface, and between this stage and the final discoid condition they never assume either the polycotyledonary or zonary mode of arrangement. Hence every Human placenta, during its own development, illustrates the direct evolution of the discoid out of the diffused arrangement.

As I described, in my last year's course of lectures on the placenta[1], the various gradations as regards deciduation and non-deciduation during the act of parturition exhibited by the zonary, polycotyledonary, and diffused forms of placenta, I need not dwell further on them on this occasion. With regard to the dome-shaped placenta, in the Sloth it is undoubtedly deciduate, though in the *Myrmecophagidæ* its condition has not yet been precisely ascertained. The several examples of discoid placenta, so far as they have been studied, also furnish well-marked examples of the deciduate placenta.

Though we are enabled, by the study of the structure of the placenta in different mammals, to conceive how, by comparatively slight modifications in the arrangement of the fœtal and maternal parts of the organ, a highly specialized placenta may have been evolved out of a simple and more generalized form, the question of what it was that induced this evolution to take place is one of much greater difficulty, and in the present state of biological science impossible to solve.

There can be little doubt that organisms may become modified by the direct action of surrounding agencies, and

[1] See my published *Lectures on the Comparative Anatomy of the Placenta*, 1st series, Edinburgh, 1876.

further, that, through the operation of these agencies on the organism, actions may be set up which re-act on the matter of the organism itself. Thus changes in climate, food, and the character of the habitat of an organism may induce variations in the tegumentary organs, the teeth and other portions of the digestive apparatus, the limbs and the skeleton, which variations may be perpetuated, in the descendants of the individual in which they may arise, by hereditary transmission, or may even become more and more pronounced in successive generations, if they should prove useful to the life purposes of the individual and of the species.

But the conditions generally under which the placenta is placed in all mammals seem to be so nearly uniform, that it is difficult to see how it can be affected by surrounding agencies. In all mammals the placenta is enclosed in a uterus, situated in the abdominal cavity: it is at a uniform temperature, so that it cannot be affected by variations in the amount of external heat, and it is altogether excluded from the action of light. Whether its form be diffused or concentrated into a more limited area, it has to perform the same function, viz. that of preparing material for the nutrition of the fœtus, and of bringing that material into sufficiently close relation to the fœtal vascular system so that it may be readily absorbed. Although it is possible that the structural modifications, which I have described, may influence the rapidity of transmission of material from mother to fœtus, there can be little doubt that the chemical and osmotic changes which go on in the several forms of placenta are similar in all cases.

It may be of some interest, however, to consider more in detail some of the special conditions in which the placenta is placed, and to enquire if the habits of life of the animal, the duration of gestation, the size of the mother and fœtus, the shape of the uterus, the number of fœtuses produced at a birth, or the relative size and distribution of the allantois, can have exercised any influence in producing modifications in the form and minute structure of the placenta.

As the discoid and zonary forms of placenta occupy a much smaller proportion of the chorion than do the polycotyledonary

and diffused, the modification in shape and the consequent concentration of the organ in a more limited area in the disco- and zono-placentalia might be supposed to be correlated with certain habits of life, which rendered it advisable that the placenta in them should be packed in a comparatively small space.

Thus it might be thought that speed was not so compatible with the possession of a large diffused, as with a compact discoid placenta, or that an animal might climb or burrow more readily if its placenta were limited in its area, and occupied a smaller proportion of the abdomen. But a comparison of the habits of the mammalia with their placental characters does not bear out this supposition. The Horse, one of the swiftest of terrestrial mammals, and the *Balænoptera* of aquatic mammals, have the diffused placenta alike with the lumbering Pig and Hippopotamus; whilst the Deer and Antelope with the cotyledonary placenta have an equal, if not greater speed than the zono-placentary Dog or Lion which chases them. The Hedgehog, which rolling itself up into a ball lies torpid for many months of the year, has a discoid placenta, like the Bat, which in its flight flits as rapidly before the eye so as to produce scarcely any image of its form on the retina. The Lemur with its diffused placenta is as arboreal in its habits as the Squirrel or Monkey with their discoid placenta. The Hare which lives and runs on the surface of the ground has a discoid placenta like the Rabbit and Mole which burrow and tunnel out passages under the surface.

There are considerable differences in the duration of gestation, and consequently in the rate of development of the tissues and organs in different mammals, and it is a fair subject for enquiry if a short gestation and rapid histological development are invariably associated with one form of placenta, a long gestation and slower development with another; but here also there is no definite relation between the habit and the anatomical arrangement. The disco-placentary Rabbit has a gestation of four weeks, whilst the Human female, also with a discoid placenta, has one of nine months. The zono-placentary Cat has a gestation of eight weeks, the Lion of fourteen weeks, and the Elephant of nearly two years. The

Sheep with its cotyledonary placenta goes twenty-one weeks with young, whilst the Cow with a similar placenta is pregnant for nearly double that period. The Llama, with a diffused placenta, has a gestation of twenty-four weeks, whilst the Mare carries its young for eleven months, and the Camel for thirteen months.

As some mammals are much larger than others, and as the fœtus at the time of birth bears a proportion to the size of the mother, it might be thought that the smaller, more compact placentæ would be found in those animals in which the fœtus attains no great size, and the more diffused placentæ in the bigger species, and to some extent this is undoubtedly the case. Thus many of the smaller mammals, as the Rodents, Bats and *Insectivora* have a discoid placenta, and a zonary placenta is found in the smaller *Carnivora*. But the zonary placenta is also present in the larger *Carnivora*, and in the Elephant, the biggest of all existing terrestrial mammals, whilst a discoid placenta occurs in the Human female. Although a diffused placenta is met with in the huge *Balæna* and *Balænoptera* amongst the *Cetacea*, and in the Hippopotamus, Tapirs and Camels amongst land mammals, whilst the Giraffe, Oxen and Deer have the polycotyledonary form; yet in these groups also smaller species are found with similarly formed placentæ; thus the Chevrotains and Peccaries have a diffused placenta, and the little Musk deer a cotyledonary.

Another point which needs consideration in the discussion of this question is the relation between the shape of the uterus and the form of the placenta. To some extent there does seem to be a relation, although exceptional arrangements occur. Uteri, as is well known, are either simple, *i. e.* possess a single cavity, or are divided into two horns. Now it would appear that the diffused, polycotyledonary and zonary forms of placenta never occur in a simple uterus, but the discoid placenta is met with both in simple and bicornuous uteri.

There is also no definite relation between the form of the placenta and the number of fœtuses produced at a birth. The Mare, the *Cetacea*, the Lemurs, the *Manis* amongst the mammals with a diffused placenta are uniparous, but the Pig, also with a diffused placenta, may produce at a birth ten or a dozen or even more. The *Carnivora* as a rule have several young at

a birth, but the zono-placentary Seals and Elephant carry only a single fœtus. The disco-placental Rabbit, Mole, and Hedgehog are pluriparous, whilst the Hare, Monkey and Human female are uniparous. In a uniparous mammal, with a diffused or polycotyledonary placenta, the chorion is not limited to the horn of the uterus in which the fœtus is lodged, but extends to the tip of the opposite horn: in the zono-placental uniparous Seal, with a two-horned uterus, the chorion is limited to the fecundated cornu; in the disco-placental uniparous Hare the chorion extends into the non-fecundated horn. But, for the purposes of the placenta, one of the compartments of the uterus in a pluriparous mammal may be regarded as the equivalent of the entire uterus of a uniparous mammal.

As the chorion derives its vascularity from the allantois, and as the distribution of the allantois over the inner surface of the chorion determines the extent of the vascularity of that membrane, it might have been thought that the villi would persist over the whole of the chorion to which the allantois proceeded, so that the form of the placenta would be regulated by the arrangement of the allantois; that in the diffused placenta, for example, the allantois would be much more extensively distributed than in the discoid, and that the disappearance of villi from the surface of the chorion would be associated with an atrophy of the vessels of the allantois. The Human placenta would indeed seem to give support to this view, for at an early stage of development the vascular allantois is distributed over the whole inner surface of the villous chorion, though in the later stages its vessels disappear over an extensive area, the villi of which also atrophy. But the comparative examination of the placenta shows this to be by no means the general rule, for in the diffused placenta of the Pig the poles of the chorion are vascular, though they are non-villous; in the polycotyledonary placenta the intercotyledonary parts of the chorion, though non-villous, are yet highly vascular, and in the zonary placenta the poles, though free from villi, have an abundant capillary plexus distributed in them. Neither can the persistence of the sac of the allantois have any influence in determining the persistence of the villi on the surface of the chorion, for the *Cetacea*, though with the villi diffused over almost the entire

outer surface of the chorion, have the sac of the allantois restricted to that part of the chorion which lies opposite the belly of the fœtus.

No one of these several conditions can in itself be regarded as furnishing a sufficient determining cause capable of accounting for the production of the different forms of placenta, and as two or more do not occur together in a sufficiently definite manner to permit us to say that in combination they may produce the variations met with, we are, so far as these agencies are concerned, still ignorant of the true causes of the modifications in the placenta. That some advantage in the economy of the organ has resulted to the animals possessing a discoid or zonary placenta from their concentration in a limited area, over those mammals which retain the less highly specialized diffused and polycotyledonary forms, is very probable. The dilatation of the maternal vessels into colossal capillaries or into sinuses, which seems to be general in the zono-placentary mammals, which exists also in the lobes of the dome-shaped placenta of the Sloth, and in Man and Monkeys amongst the disco-placentalia, modifies the relation of the maternal vessels, with their investing epithelium, to the fœtal villi. In the diffused and polycotyledonary placentæ, which possess a maternal network of ordinary capillaries, only one aspect of the maternal vessel is in relation to the maternal epithelium and the fœtal villi; but, in the other placentæ referred to, the entire circumference of the maternal vessel is surrounded by maternal epithelium and fœtal villi, which would seem to permit of a more rapid interchange of material between the mother and the fœtus; just as in the lungs of birds and mammals the pulmonary capillaries are arranged so as to have their wall more completely in relation to the air in the air-sacs than is the case in the lungs of reptiles.

We have no definite information before us for determining if the surface of the chorion covered by villi varies in its extent inversely with the length, absolute number and complexity of the villi springing from it. We certainly do know that in the diffused placenta the villi though numerous are short and simple, whilst in the more concentrated forms, though fewer in number, they have increased in length or breadth, and in

the complexity of their ramifications; but we cannot say if the increase in their length, breadth and complexity bears a precise relation to the diminution in the extent of the horizontal area of the chorion from which they spring. It is possible that the concentration of the villi within a disc or zone may, by limiting the horizontal area of the organ, require the expenditure of a smaller amount of force in the placental circulation than when the placenta is diffused over an extensive surface, and that the flow of the blood, through dilated capillaries, or irregular sinuses, may be accompanied by a smaller amount of friction than when it flows through an ordinary capillary plexus. Should this be the case, then the physics of placental nutrition and circulation would undoubtedly gain something by these modifications in arrangement; and their production, at some remote epoch, as a variation arising in some animal or animals, may, through an advantage in the economy of the organ, have led to their perpetuation by hereditary transmission.

We do not and indeed cannot expect ever to know anything of the placentation of extinct mammals, for the rocks have borne no testimony to the shape and structure of this organ. We may assume, perhaps, as a matter of speculation, that the extinct mammalia, which in their osteological characters so far resembled existing animals as to be referred to the same families and genera, possessed a placenta similar in form and structure to that present in the allied existing animals.

It does not appear that any of the existing genera of mammals have been traced further back in geological time than the miocene division of the tertiary period, though many can only be followed into the pliocene[1].

Amongst the *Perissodactyla,* for example, remains of the Horse have been found in pliocene formations, together with those of certain horse-like animals, which have been named *Protohippus, Merychippus* and *Hipparion;* whilst the North American genera *Mesohippus* and *Miohippus* prolong the line

[1] I may refer to the excellent Lectures of Professor Flower for much valuable information on the antiquity and the affinities of the extinct mammalia, as deducible from a comparison of their osteological characters. See *Proceedings of Royal Institution of Great Britain,* April 25, 1873, and March 10th, 1876; also *Nature,* Feb. 17th to May 4th, 1876.

back through the miocene to the *Orohippus* of the eocene period. The Rhinoceroses go back to the pliocene and through the American genera *Diceratherium* and *Hyracodon* to the miocene;. whilst the Tapirs have also been met with in the miocene. But in the early miocene and eocene the remains of animals are found, which in their skeletons combined the characters of the existing genera of *Perissodactyla*. Thus the *Anchitherium* possessed both horse and tapir-like characters, the *Palæotherium* had arrangements suggestive of the rhinoceros, horse and tapir, whilst the *Lophiodontidæ* of the early eocene formed apparently a more generalized ungulate type.

Now as existing horses, tapirs, and probably rhinoceroses have a diffused placenta, and on the assumption that the diffused placenta is the least specialized form, it is not unlikely that the extinct *Perissodactyla* had also a diffused placenta, though in the *Lophiodontidæ* it may have closely approximated to the generalized type of placenta.

Amongst the *Artiodactyla* the tubercular-toothed division, or Bunodonts, possess considerable antiquity. The pigs go back to the later miocene and the hippopotamus to the pliocene. The existing genera have, and the extinct forms probably also possessed, a diffused placenta. The Selenodont, or ruminant *Artiodactyla*, have been found in the pliocene and later miocene. The more typical existing ruminants have, as is so well known, the polycotyledonary placenta, a form which was probably possessed by their miocene and pliocene ancestors. In the North American miocenes the family *Oreodontidæ*, and in the later eocenes the genera *Anoplotherium*, *Dichobune*, *Chæropotamus* and *Hyopotamus* are found, which partake of the characters of both pigs and ruminants. These genera are also allied to the true pigs through the transitional forms *Chærotherium* and *Palæochærus;* so that genera at one time existed which combined the characters of those families of Artiodactyles, some of which we now know to possess a diffused, others a polycotyledonary placenta. It is probable that in these extinct forms the placenta was diffused, though beginning, it may be, to put on the cotyledonary arrangement. But amongst existing ruminants two aberrant forms, the Chevrotains and Camels, possess the diffused placenta. Through the Chevrotains the

Ruminants gravitate towards the Bunodonts or pigs, whilst through the Camels they incline, through the extinct genus *Macrauchenia*, to the *Perissodactyla*. Not only therefore do extinct forms supply transitional links between the true ruminants and those extinct genera in which presumably the diffused type of placenta was present, but amongst existing ruminants are found genera, which, possessing the diffused type of placenta, are allied in the one case to the diffused placental Perissodactyles, in the other to the Bunodonts. Hence it seems to me that the palæontological evidence supports the argument which I had previously based on a consideration of their structural characters, that the polycotyledonary placenta, which is only a little more specialized than the diffused placenta, may have been evolved out of a more generalized diffused form.

The diffused placenta is not however limited to the *Ungulata*, but, as we have already seen, is found in the *Cetacea* and Lemurs. The palæontological history of the *Cetacea* carries them back to pliocene and miocene times, and if *Zeuglodon* is to be regarded as an ancestral form of the order, even to the eocene. There is distinct evidence that Lemurs existed in the early miocene, and possibly even in eocene times. Presumably the *Cetacea* and Lemurs have preserved the simple diffused placenta through all these ages; though the concentration of the gland-openings in large areas in the uterine mucosa of existing Lemurs marks a greater degree of specialization, than if each gland had opened independently in its own area, as is the case for example in the common pig, and as may perhaps have been the arrangement in the more ancient forms of Lemurs.

Of the zono-placental mammals the *Proboscidea*, *Canidæ*, *Viverridæ* and *Felidæ* can be traced through the pliocene to the miocene period, whilst the remains of Bears and Otters do not appear to have been found older than the pliocene. When the process of specialization of a zonary placenta first began we have no evidence. But the differentiation as regards the *Proboscidea* may perhaps have originated in some of those gigantic forms included under the name of *Dinocerata*, which have recently been discovered in the American eocenes, and which as Professor Flower has stated seem to bridge over the gulf between the modern orders of *Proboscidea* and Perissodactyle Ungulates. And in support of this view I may recall

attention to the observation made twenty years ago by Prof. Owen on the placenta of the Elephant, in which he saw not only the zonary equatorial band, but a patch of villi diffused over the chorion at each of its poles. These diffused patches preserve in the placental structure evidences of the perissodactyle affinities of the modern *Proboscidea*.

The remains of mammals exhibiting affinities with existing *Carnivora* have been found in the eocene, as the *Arctocyon primævus*, the different species of *Hyænodon*, and the genera *Synoplotherium* and *Mesonyx*, whilst the miocene has yielded certain generalized types, as the *Amphicyon*, which seems to combine the characters of modern dogs and bears, and the *Machærodus*, which is allied to the *Felidæ*. It is possible that in these extinct genera, the differentiation into a zonary placenta may have occurred; though the affinities of the extinct *Zeuglodon*, on the one hand with the Seals, and on the other with the *Cetacea*, may indicate that to be the line through which the differentiation has been effected. On the other hand, such genera as *Hyænodon*, *Synoplotherium* and *Mesonyx*, which possess affinities in some of their skeletal characters with the *Insectivora;* or those genera, which Professor Marsh has grouped together in the order *Tillodontia*, and which combine the characters of Carnivores, Ungulates and Rodents, may indicate the direction along which the discoid form of placenta may have originated.

Of the disco-placental mammals, existing families of *Rodentia*, *Insectivora* and *Cheiroptera* have been found in the miocene, but remains allied to these orders have been described from eocene strata. No very reliable evidence of the remains of true Monkeys has been obtained older than the miocene. Whether the differentiation of the discoid placenta took place in miocene times, or at some earlier period in connection with then existing genera, it is of course impossible definitely to state; though from the fact that the osteological and dental characters of these orders were distinctly differentiated, the placental characters were in all probability likewise differentiated in the miocene period, so that the production of the discoid placenta had presumably taken place at an earlier epoch.

From the description which has been given in these lectures of the form and structure of the placenta it will have been seen

that in the genera constituting several of the orders and sub-orders of mammals the placenta has an uniform shape, and within certain limits a close correspondence in internal structure, so that their placental affinities correspond with affinities in the other organic systems. Thus the *Perissodactyla* possess a diffused placenta, the typical Ruminants a polycotyledonary placenta, the *Carnivora*, including the *Pinnipedia*, a zonary placenta, the *Rodentia*, *Insectivora*, *Cheiroptera*, Monkeys and Man each a discoid placenta. On these grounds a classification of the Mammalia on the basis of the placenta has been proposed and adopted by many zoologists. But with this system of classification, as with other systems, which have been based on the characters of a single organ, though it may be found applicable to many genera, yet exceptions occur in such numbers, and of so much importance—exceptions so difficult to reconcile with the general basis of the system—that in my opinion the placental system of classification can no longer be sustained.

Thus in the order *Artiodactyla*, whilst the bunodont Pigs and Hippopotamus have a diffused placenta, the typical Ruminants have a polycotyledonary placenta; though in the aberrant Camels and Chevrotains the placenta is as diffused as in the bunodonts; whilst in the Giraffe, the placenta, though chiefly cotyledonary, yet has to some extent villi diffused over the surface of the chorion. But in the order *Edentata*, as at present constructed, a more remarkable diversity in placental form is met with. In *Manis* the placenta is diffused. In the Hairy Ant-Eaters and Sloths it is dome-like; a similar arrangement, judging from Kölliker's[1] description, is met with in the Armadilloes, though Owen describes the placenta in *Dasypus* as a single, thin, oblong, disc[2]; whilst in *Orycteropus*, as I have recently shown, the placenta is broadly zonular[3], so that the *Edentata*, so far as their placentation has been up to this time studied, furnish examples of all the known group-forms of placenta, except the polycotyledonary. It may, however, be said that the *Edentata* form an order constituted on no very definite basis; that they are animals associated together on the ground of possessing certain negative characters in common, rather than from any positive affinities, and that no

[1] *Entwicklungsgeschichte des Menschen*, 2nd ed. p. 362, Leipzig, 1876.
[2] *Comp. Anat. Vertebrates*, III. p. 731. 1868.
[3] This *Journal*, July, 1876, p. 693.

argument of any weight, as against the placental system of classification, can be based on the diversities of placental form and structure which they exhibit.

But the differences in the *Edentata* and *Artiodactyla* are not the only obstacles to accepting the placental system of classification. The genus *Hyrax*, for example, presents an organisation so remarkable, that whilst some zoologists have referred it to the *Rodentia*, others have regarded it as allied to the *Ungulata;* others have looked on it as intermediate between Ungulates and Rodents; others have made it the type of a distinct order *Hyracoidea*, having affinities on the one hand with the *Ungulata*, on the other with the *Rodentia* and *Insectivora*. But this animal, as indeed has long been known, has a placenta which is neither diffused, nor polycotyledonary as in the *Ungulata*, nor disc oid as in the *Rodentia* and *Insectivora*, but zonary as in the *Carnivora*. Moreover, as I ascertained from the examination of a specimen a few months ago[1], the minute structure of the placenta of *Hyrax* is so like that of the domestic cat, that it is difficult to distinguish the one from the other. In its placental, though not in its other affinities, *Hyrax* approaches so closely to the *Felidæ*, that, if the placenta is to be regarded as the dominant character in classification, it ought to be associated with the Cats, a position in which no zoologist has ventured to place it.

Again, if the form of the placenta in the genus *Elephas* were alone to be taken into consideration, the great preponderance of its equatorial zone would, on the placental system of classification, require this animal to be approximated to the *Carnivora*, an alliance which is not supported by the examination of other features of its structure.

But the Lemurs throw yet greater difficulties in the way of accepting the placental system of classification. The external form of these animals, more especially the configuration of the hands and feet, and the characters of the skeleton and teeth, have led zoologists to associate them with the higher mammalia. Linnæus grouped them with Man, Apes, and Bats in the order *Primates*, and although the Bats have by common consent been since referred to a separate order, yet many eminent zoologists retain the Lemurs with Man and Apes amongst the *Primates*.

[1] *Proc. Roy. Soc. London*, Dec. 16th, 1875.

Blumenbach and Cuvier constructed the order *Quadrumana* for the Apes and Lemurs, an arrangement which has also met with much acceptance. Gratiolet, Gervais, Haeckel, and Carus have placed the Lemurs in a separate order, one however which they regard as allied to the Apes and *Insectivora*. By all zoologists, therefore, they are considered to have close affinities with those mammals which have a discoid placenta; so close indeed has this affinity been supposed to be, that the Lemurs have been erroneously assumed to possess a disc-shaped placenta.

But the figures published by Professor Alphonse Milne Edwards[1] and the examination made by myself[2] of the gravid uteri of several genera of Lemurs have shown that in these animals the placenta is diffused, so that in their placental form and structure, as well as in the large and persistent sac of the allantois, they correspond closely with the *Perissodactyla*, bunodont *Artiodactyla*, and *Cetacea*.

Hence, if the placental characters are to out-weigh those presented by other organs, the position of the Lemurs in the class Mammalia must be completely reversed. Instead of being grouped in more or less close relationship with the Apes and *Insectivora*, they must be placed alongside of the Whales and *Ungulata*. But this is a position which will, I think, scarcely be accepted by zoologists.

From a consideration therefore of the form and structure of the placenta in the several orders of mammals, so far as we have as yet had an opportunity of studying it, one is led to the conclusion that, for purposes of Classification, the placenta cannot be accepted as a dominant organ; but that in the present state of science, where our acquaintance with the genealogical relations of animals is insufficient for the construction of a definite pedigree, the presence of a combination of similar characters drawn from more than one system of organs gives a safer guide to the affinities of an animal, than the existence, in only a single organ or system, of even a very close resemblance in form and structure.

[1] *Histoire Naturelle des Mammifères de Madagascar*. Vol. IX. Tome IV. Atlas I. Plates 118 to 121. No description of these plates has yet been published. Paris, 1875.

[2] *Trans. Roy. Soc. London*, 1876.

ON THE STOMACH OF THE FRESH-WATER CRAYFISH. By T. J. PARKER, *Assoc. R.S.M., Demonstrator of Biology in the Royal School of Mines.* Pl. II.

(*From the Biological Laboratory of the Royal School of Mines.*)

THE Stomach of the Crustacean with its curious gastric mill has been described by Oesterlen ("Ueber den Magen des Flusskrebses," Müller's *Archiv*, 1840), Milne-Edwards (*Histoire naturelle des Crustacées*, Tom. I.), and Huxley (*Med. Times and Gazette*, March 4th, 1857): a few points, however, seem to have been overlooked, and to these I wish to draw attention.

The stomach of the Crayfish is a large chamber, situated in the cephalic region of the animal, and distinctly divided, by a constriction, into an anterior cardiac, and a posterior pyloric division (Pl. II. figs. 2 and 3). It is composed of a delicate cellular membrane, lined by a strong chitinous layer, by the calcification of certain parts of which the masticating apparatus or gastric mill is produced.

In the roof of the globular cardiac portion of the stomach is a strong transverse bar of calcified chitin (*c*), the "pièce cardiaque" of Milne-Edwards, or "Querbalken" of Oesterlen. The lateral edges of this *cardiac ossicle* are cut obliquely, so that, if produced, they would meet at a point slightly behind the anterior boundary of the stomach: from the centre of its hinder border is continued backwards and downwards a median *urocardiac process* (*u. c.*) ("pars quadrata," Oesterlen) which, although calcified, is so elastic, as to be moveable vertically about its junction with the cross-bar. The posterior extremity of this median process is thickened, and produced inferiorly into two small toothlets, the *accessory teeth* (*a. t.*) ("cardiac teeth," Huxley). With each obliquely-cut extremity of the cross-bar, a small sub-triangular *ptero-cardiac ossicle* (*p. c.*) ("S-förmige Knöchelchen," Oesterlen; "pièce ptéro-cardiaque," Milne-Edwards) is connected.

The urocardiac process articulates posteriorly with the *prepyloric ossicle* (*p. p.*) ("Pars triangularis," Oesterlen: "pièce pylorique antéricure," Milne-Edwards), which is situated in the

front wall of the pyloric dilatation, and takes a direction upwards and forwards, so as to include, in the quiescent condition of the apparatus, an acute angle with the urocardiac process. The pre-pyloric ossicle is broad above, narrows gradually towards its lower end, and then suddenly expands, and constitutes a kind of cup, the posterior face of which forms a continuous sigmoid curve with the pre-pyloric ossicle itself (see Fig. 3), while the anterior lip projects forwards, and furnishes the articulation for the urocardiac process. The cup thus formed has its walls greatly thickened and of a horny appearance, and, projecting into the cavity of the stomach, forms the strong, bifid *median tooth* (*m. t.*) ("Mittelzahn," Oesterlen: "urocardiac tooth," Huxley). Oesterlen describes this tooth as being formed behind by the pre-pyloric ossicle, and in front by a small separate piece intercalated between it and the end of the urócardiac process: Professor Huxley (*loc. cit.* p. 255) describes it as being borne entirely by a separate ossicle. This is probably owing to the fact that there is a transverse mark on the dorsal side of the urocardiac process, producing the appearance of a separation, which, however, a longitudinal section shows not to be a real one.

In the roof of the small pyloric dilatation of the stomach is situated the *pyloric ossicle* (*p*) ("Sattel," Oesterlen), a transversely arcuated plate articulating anteriorly with the upper end of the pre-pyloric piece, with which it forms an acute angle, and, on each side, becoming continuous with the posterior extremity of a stout calcification (*z. c.*), developed in the side-walls of the cardiac portion of the stomach, which articulates, in front, with the backwardly curved slender end of the pterocardiac ossicle. This is the "Seitenwandknochen" of Oesterlen, or "pièce latérale supérieure" of Milne-Edwards; as, however, it constitutes one of the chief parts of the gastric mill, and needs therefore to be distinguished from certain other calcifications which simply support the walls of the stomach and give attachment to its intrinsic muscles (*vide infra*), it will be better to speak of it as the *zygo-cardiac ossicle*. The inner border of this ossicle is flanged horizontally inwards, and forms the great serrated *lateral tooth* (*l. t.*), which projects so far into the cavity of the stomach, as to be a very short distance from the median

tooth even in the position of rest of the organ. When, however, the cardiac and pyloric ossicles are pulled respectively forwards and backwards—as they are pulled by the gastric muscles mentioned below—a great change in the disposition of the parts ensues. The pre-pyloric ossicle assumes a vertical position, including, now, a right angle with the pyloric piece, the urocardiac process bends downwards, the median tooth becomes vertical, the zygo-cardiac ossicles are pulled backwards dragging with them the lower ends of the ptero-cardiacs, which, by reason of their oblique articulation, are constrained to move not only backwards, but inwards and downwards: the same inward and backward motion is, consequently, given to the front ends of the zygo-cardiacs, so that the lateral teeth, approaching the middle line, come into contact with the median tooth, and grind against it with considerable force.

Besides the six ossicles forming the gastric mill, there are several accessory calcifications both in the cardiac and pyloric parts of the stomach. These are all described by Milne-Edwards (*l. c.* p. 68), who calls them pièces cardiaques postérieure, latérale-inférieure (Fig. 2, *i. l.*), latéro-postérieure (*p. l.*), latérale, and latérale-accessoire (*a. l.*); and pièces méso-pylorique (*m. p.*), uro-pylorique, pylorique latérale (*l. p.*), and pylorique inférieure. Of these only the "pièce cardiaque latérale" need be more than mentioned: it expands below into a large oval cartilaginous plate, and bears a small, pointed *infero-lateral tooth* (Figs. 2 and 3, *i. l. t.*), which projects into the cavity of the stomach over against a little projection (*t′*) on the lower border of the great lateral tooth.

The complicated valvular arrangements in the cardio-pyloric and pyloric regions of the stomach are described by Professor Huxley (*loc. cit.* p. 255).

In the Lobster the gastric apparatus differs in no important respect, except in size, from that of the Crayfish: of minor points of difference the chief are the rudimentary condition of the accessory teeth, and the fact that the median tooth has a single blunt point.

In the Crab, which is taken as a type by Milne-Edwards, the cross-beam of the cardiac ossicle is reduced almost to nothing, the ptero-cardiacs, at the same time, becoming very

large: the uro-cardiac process is of great length and forms a separate ossicle, and on it, instead of on the pre-pyloric ossicle, the median tooth is found. In consequence of these arrangements, and of the loose mode of articulation of the various pieces, the gastric mill of the Crab is—as a cursory examination will show—a far less perfect masticatory apparatus than that of the Crayfish or Lobster, although possessed by a more specialised animal.

The muscles with which the stomach is provided may be divided into two sets, an extrinsic and an intrinsic. In each set some muscles have to do with the movement of the gastric mill, while others are concerned in the movements of the stomach as a whole.

In the extrinsic set, there are, first of all, the gastric muscles proper, of which there are two pairs, an anterior and a posterior. The anterior pair (Fig. 1, *a. g.*) arise from the base of the rostrum or procephalic process (*pc. p.*), and are inserted into a cartilaginous plate ("Decke," Oesterlen) into which the front edge of the cardiac ossicle is produced, and somewhat in front of the latter. The posterior pair (*p. g.*) arise from the inner surface of the roof of the carapace, somewhat behind the posterior boundary of the stomach, and are inserted into the pyloric ossicle and the posterior ends of the zygo-cardiacs. When these muscles contract together, they pull apart the cardiac and pyloric ossicles and, as mentioned above, bring the teeth of the mill into contact. As a matter of fact they are the only muscles which are of any importance in the working of the apparatus, for (see Huxley, *loc. cit.* p. 255) when they cease to contract it returns to the position of rest by its own elasticity.

The remaining extrinsic muscles are of small size, and amount altogether to nine pairs. Two pairs, the *anterior dilators* of the stomach (Fig. 1, *a. d.*) arise, on each side, from the antennary sternum, and pass directly backwards, between the circum-œsophageal nerve-commissure and the azygos stomato-gastric nerve, to their insertion in the front wall of the stomach and œsophagus. Three pairs of *lateral dilators* (*l. d.*) arise from the mandibular sternum, and pass inwards and backwards, immediately in front of the *adductor mandibulæ* muscle, to the side-walls of the stomach and gullet. An-

other pair of lateral dilators (*l. d'.*) arise from the outwardly-curved, anterior horns of the intermaxillary apodeme, and pass almost directly forwards to the walls of the œsophagus. Two pairs, the *inferior dilators*, arise, the larger (*i. d.*) from the internal thickened edge of the dorsal surface of the mandible, the smaller (*i. d'.*) from the upper surface of the intermaxillary apodeme (*i. m. a.*), and pass upwards and slightly backwards to be inserted into the inferior pyloric ossicle. Lastly, a pair of *superior* or *pyloric dilators* (*s. d.*) arise from the carapace immediately behind the point of origin of the posterior gastric muscles (where there is in the Lobster, though not in the Crayfish, a little calcareous projection for their attachment) and pass downwards, close together, to their insertion in the upper surface of the pyloric dilatation, a little in front of the dorsal cœcum of the intestine. The anterior dilators are mentioned by Dr Rolleston at p. 100 of his *Forms of Animal Life*, and the inferior dilators by Milne-Edwards (*l. c.* p. 71): there is, however, no description of the muscles given by either of these writers, and of the remaining fasciculi I have met with no notice whatever.

All these lesser extrinsic muscles, at any rate when acting together, must serve to increase the cavity of the stomach. The attachment of the larger pair of inferior dilators (*i. d.*) is very curious, for passing, as they do, between the mandible and the stomach, they must tend to pull down the latter every time the mandibles are divaricated. They might, perhaps, assist slightly in mastication, by raising the inner edges of the mandibles, and so bringing their toothed surfaces into contact, if the stomach were kept fixed by the contraction of the posterior gastrics and superior dilators, but they are too feeble to be of any real assistance to the enormous *adductores mandibularum*.

The intrinsic muscles are developed between the two layers of the stomach, and are easily seen when the delicate external layer is dissected off. One pair (Fig. 1, *c. p.*) are found on the upper surface, passing between the side pieces of the cardiac and the posterior ends of the zygo-cardiac ossicles, into which their anterior and posterior ends are respectively inserted. They are consequently put on the stretch when, by the action of the great gastric muscles, these two ossicles

are separated, and, on the gastrics ceasing to act, will, by their contraction, act as weak antagonists to the latter, and assist in bringing the apparatus to its position of rest. This action must, however, in the Crayfish and Lobster, be extremely feeble, as they are very delicate, probably not more than one layer of muscular fibres thick. In the Crab, on the other hand, where the mechanical advantages are much less, one was naturally led to expect that these *cardio-pyloric muscles* would take on a greater development, and this is actually the case. An azygos median band is developed, in addition to the pair found in the macrurous genera, and the muscles are far stouter than in the latter. These muscles, also, have, as far as I am aware, not hitherto been described.

The remaining intrinsic muscles (*cn.*) form an incomplete middle coat to the stomach, and act as "constrictors," thus antagonising the extrinsic "dilators." One set of fibres almost encircles the pyloric dilatation: others lie in the side-walls of the cardiac portion where they pass between the zygo-cardiac and infero-lateral ossicles, and between the infero-lateral and the front border of the lateral cartilaginous plate; a few are also found in front of the cartilaginous plate. Besides their constricting function it is possible that the fibres passing between the zygo-cardiac and infero-lateral ossicles may serve to bring the infero-lateral tooth into contact with the accessory denticle (*t'.*) of the lateral tooth. It also seems not altogether unlikely that the dilators and constrictors, acting alternately, may confer upon the stomach a suctorial function, such as is possessed by the buccal sac of the Scorpion, described by Professor Huxley, thus enabling the animal to take in more readily the putrid, often semi-fluid, matters on which it feeds.

EXPLANATION OF PLATE II.

Fig. 1. The stomach *in situ:* the anterior and posterior gastric muscles of the left side are cut away to their insertions: the origins of the lateral dilators and of the chief inferior dilators are also removed.

Fig. 2. The stomach with the external coat removed; the median and lateral teeth are seen through the transparent inner coat.

Fig. 3. A longitudinal vertical section of the stomach.

Fig. 4. The ossicles of the gastric mill, disarticulated and viewed from the ventral aspect.

References.

a. d. anterior dilator muscles.
a. g. " gastric "
a. l. accessory lateral cardiac ossicle.
ant. st. antennary sternum.
a. t. accessory tooth.
b. d. aperture of the bile duct.
c. cardiac ossicle.
c. gn. cerebral ganglion.
cn. constrictor muscles.
cœ. cœcum.
c. p. cardio-pyloric muscles.
c. p. v. " valve.
e. c. external coat of stomach.
i. c. internal " "
i. d., *i. d'.* inferior dilator muscles.
i. l. infero-lateral cardiac ossicle.
i. l. t. infero-lateral tooth.
i. m. a. inter-maxillary apodeme.
int. intestine.
l. d., *l. d'.* lateral dilator muscles.
l. p. lateral pyloric ossicle.
l. t. lateral tooth.
m. mouth.
m. p. meso-pyloric ossicle.
m. t. median tooth.
œs. œsophagus.
p. pyloric ossicle.
p. c. ptero-cardiac ossicle.
pc. p. procephalic process.
p. g. posterior gastric muscles.
p. l. postero-lateral cardiac ossicle.
p. œs. gn. post-œsophageal ganglion.
p. p. pre-pyloric ossicle.
r. rostrum.
s. d. superior dilator muscles.
sg. n. stomato-gastric nerve.
t'. accessory denticle of lateral tooth.
u. c. uro-cardiac process.
z. c. zygo-cardiac ossicle.

EXPERIMENTS ON THE BILIARY SECRETION OF THE DOG. By Prof. RUTHERFORD and M. VIGNAL.

Second Series.

IN the first series of our experiments we gave an account (this *Journal*, x. 253) of the action of podophyllin, colchicum, rhubarb, aloes, scammony, taraxacum, senna, calomel, gamboge, croton and castor oil on the secretion of bile in the dog. We have now to detail the actions of a number of other substances. In these experiments we have adopted precisely the same method as in the previous ones; that is to say, we have always used dogs; these being the only animals suitable for the purpose. They had always a full meal of flesh at four o'clock in the afternoon, and the experiment was begun at nine o'clock on the following morning, so that digestion and absorption had fully taken place;—a condition that is essential for obtaining a constant secretion of bile. In all cases, irregular muscular movements were prevented by small doses of curara, it having been ascertained that these have no apparent influence on the biliary secretion, nor do they prevent the manifestation of the effects of hepatic stimulants. In consequence of the curara paralysis respiration was of course maintained artificially. As before, a glass cannula was tied in the common bile-duct, the cystic duct was clamped, and all the bile secreted was thereby compelled to flow out through the cannula into a finely graduated cc. measure, where it was constantly collected and the amount observed and recorded every fifteen minutes. Each experiment usually lasted an entire day, at the close of which the animal was killed, and the alimentary canal examined. The various substances were always injected directly into the duodenum, for the reason that, in fasting dogs, the stomach is apt to contain a large quantity of mucus that seriously interferes with the certainty of the speedy absorption of the various substances administered. We therefore had recourse to the small intestine, and we preferred the duodenal portion,

in order that we might certainly bring the substance into contact with *its* mucous membrane, in case of any sympathy between it and the liver. The whole method is more fully detailed in our previous communication, but it may be well to state that in these experiments anæsthetics were not administered, because of their disturbing influence on the biliary secretion. In two of our earlier experiments we administered chloroform during the preliminary operation, but the stimulation of the liver produced thereby was so remarkable, that the animals were rendered useless for further experimentation. To avoid equivocal results, we therefore abstained from the preliminary administration of any substance other than curara.

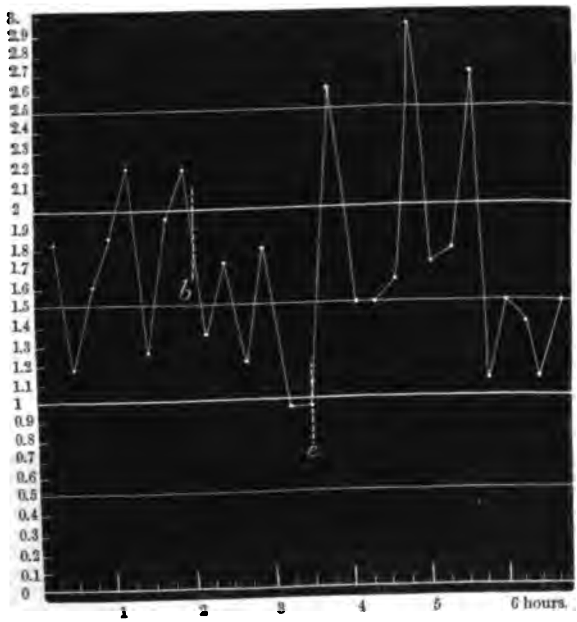
We have still confined our attention to the physiological actions of cholagogues, for it cannot be doubted that the thorough investigation of this subject is of great importance for the advance of scientific medicine.

Action of "Euonymin."

Wood and Bache in the *United States Dispensatory* for 1869 (p. 374) state that "the precise virtues of the bark of Euonymus atropurpureus have not been determined." Mr C. A. Santos—quoted by them—describes it as "tonic, hydragogue cathartic, diuretic, and antiperiodic." Dr Tidyman informed them that he had obtained useful effects from it, as an alterative of the hepatic function. Wood and Bache conclude that "on the whole its character is somewhat uncertain; and it might well form a subject of further examination." The American "Eclectics" give "Euonymin" as a mild aperient in doses of from one to two grains. The substance used by them however is a very complex substance, only a portion of which consists of the active principle—the *true* euonymin. Mr Clothier found it to produce active purgation without griping. The substance employed in our experiments is an impure resin prepared by precipitating the tincture of euonymin with water acidulated with hydrochloric acid. It was obtained from Messrs Tilden and Co. of New York.

Experiment 1. Dog that had fasted 17 hours. Weight 19 kilogrammes. (Fig. 1.)

Fig. 1.[1]



Secretion of bile before and after "euonymin." 2 cc. bile and 2 cc. water injected into duodenum at *b*. 5 grains of "euonymin," together with the above fluid, injected at *e*.

The irregularity in the biliary flow in this case was certainly owing to an irregularity in *secretion*, for the cannula was perfectly patent throughout the whole of the experiment. The irregularity did not consist in the bile being expelled in jets, as might have been expected had it been owing to contraction of the larger bile-ducts at intervals, but there was a rapid and steady flow for some minutes, and then for a while it flowed much more slowly. This irregularity of secretion was probably in large measure due to unusual traction upon the bile-duct and liver during the introduction

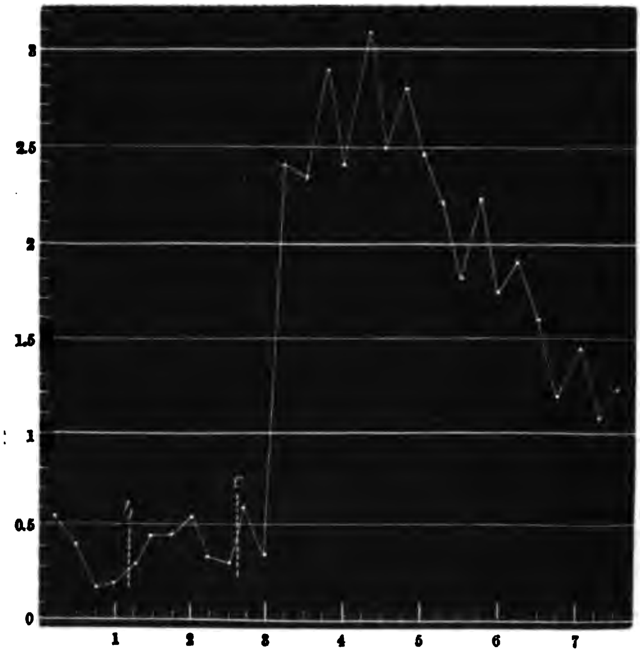
[1] Every dot in the curves in all the figures indicates the amount of bile secreted during the preceding fifteen minutes. The quantity is always expressed in cubic centimetres.

of the cannula, which in this case was much more difficult than usual. We have repeatedly observed that unless this part of the preliminary operation be conducted so as to very slightly disturb the bile-duct and its surroundings, the biliary secretion is rendered irregular. Nevertheless it is evident that in this case the "euonymin" stimulated the liver.

AUTOPSY.—There was very slight evidence of purgative action, but the mucous membrane of the upper fourth of the small intestine was much more vascular than usual.

Experiment 2. Dog that had fasted 24 hours. Weight 23.3 kilogrammes. (Fig. 2.) The unusually long fast resulted from the animal having refused to take food on the afternoon of the day preceding the experiment. It was probably owing to this circumstance that the secretion of bile was so low at the beginning of the experiment.

Fig. 2.



Secretion of bile before and after "euonymin." 1.1 cc. bile and 3 cc. water injected into the duodenum at *b*. The same with 5 grains "euonymin" injected at *e*.

AUTOPSY.—Stomach contracted, mucous membrane normal. The "euonymin" had extended along about a third of the small intestine. The mucous membrane of the upper third was extremely vascular. Mucous flakes were scattered over the surface, and the whole appearance of the membrane reminded us of the effects of podophyllin. But notwithstanding the very obvious irritation, the intestine at this part contained only a small quantity of a watery fluid. The remainder of the intestine was dry and contracted, without any signs of irritation.

Results of Experiments with "Euonymin."—1. Five grains of "euonymin," when mixed with a small quantity of boiling water and placed in the duodenum, powerfully stimulated the liver[1]. 2. Coincident with the marked action of the liver there was only a slight increase of intestinal secretion. Seeing that Mr Clothier (quoted above) found "euonymin" to be an active purgative in the human subject, these experiments suggest that the purgative effect may be chiefly due to increased secretion of bile. At any rate these experiments clearly show that this substance is worthy of receiving far greater attention in practical medicine than it has done hitherto.

ACTION OF "SANGUINARIN."

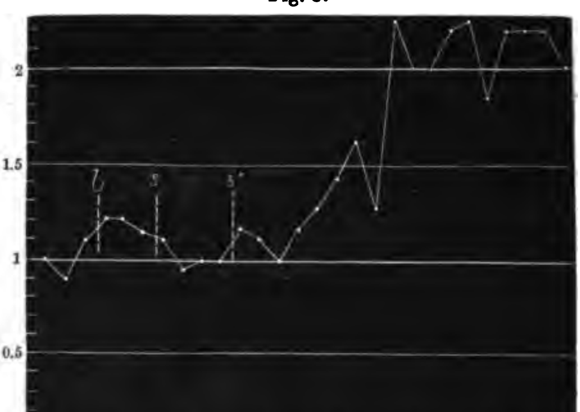
Dr Wood in his excellent *Treatise on Therapeutics* (1874) states (p. 367) that "although Sanguinaria has been used more or less for so many years, we are still without any really definite knowledge of its action. Little or nothing has been added to our knowledge since the papers by Dr Tully in 1830, who stated that when given in small repeated doses it acts as a very decided cholagogue; and more recently it has been affirmed that it is also a stimulating expectorant. In full doses it is certainly a harsh emetic, and in overdoses, according to Tully, it produces with the vomiting burning at the stomach, faintness, vertigo, dimness of vision, general insensibility, coldness, extreme reduction of the force and fre-

[1] The analysis of the bile secreted before and after "euonymin" was lost.

quency of the pulse, great prostration of the muscular strength, and sometimes a convulsive rigidity of the limbs." Dr Wood states that he has never known of its employment except as a stimulant expectorant in obstinate bronchitis. Dr Mothershead of Indianapolis (quoted in Wood and Bache's *United States Dispensatory*, 1869, p. 741) however "speaks in the strongest terms of its efficacy as an excitant of the liver, when given in alterative doses." On the other hand, Prof. Thomas, of Philadelphia (quoted by Wood and Bache, *lib. cit.*, p. 742), found the active principle sanguinarina to "have no effect of any kind directly on the liver" of man. "Sanguinarin" is however recommended by the American "Eclectics" in doses of $\frac{1}{4}$—1 grain as a hepatic alterative. The substance employed in the following experiments is a resin prepared in the same manner as euonymin (see p. 62).

Experiment 3. Dog that had fasted 17 hours. Weight 27.7 kilogrammes. (Fig. 3.)

Fig. 3.



Secretion of bile before and after "sanguinarin." 2 cc. bile and 2.5 cc. water injected into the duodenum at *b*. 1 grain "sanguinarin" in the same fluid injected at *s*. 2 grains "sanguinarin" in the same fluid injected at *s'*.

AUTOPSY.—Mucous membrane of upper two-thirds of small intestine was of a clear claret colour, here and there it was marked by brownish patches of a size varying from that of a

sixpence to that of a half-crown. There were 35 cc. of a thick brown fluid in the small intestine. The brown colour was apparently owing to the presence of the "sanguinarin," a substance of a brownish-red colour.

Experiment 1.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.82	
	1.2	
	1.6	
	1.85	
	2.2	
	1.3	
	1.95	
	2.2	
b	—	
	1.35	
	1.7	
	1.2	
	1.8	0.2578 cc.
	0.95	
	0.95	
e	—	
	2.6	
	1.5	
	1.5	
	1.6	
	2.95	
	1.7	0.4789 cc.
	1.75	
	2.7	
	1.1	
	1.5	
	1.4	
	1.1	
	1.5	

Experiment 2.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.55	
	0.4	
	0.2	
	0.21	
	0.3	
b	—	
	0.45	
	0.45	
	0.55	0.0708 cc.
	0.35	
	0.3	
e	—	
	0.6	
	0.35	
	2.4	
	2.35	
	2.9	
	2.4	0.4678 cc.
	3.1	
	2.5	
	2.8	
	2.45	
	2.25	
	1.75	
	2.25	
	1.6	
	1.85	
	1.6	
	1.2	
	1.45	
	1.1	
	1.25	

Experiment 3.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.0	
	0.9	
	1.1	
b	—	
	1.2	0.1678 cc.
	1.2	
	1.15	
s	—	
	1.1	
	0.95	
	1.0	
	1.0	
s′	—	
	1.15	
	1.12	
	1.0	
	1.15	
	1.25	
	1.4	
	1.6	
	1.25	
	2.22	
	2.0	
	2.0	0.3089 cc.
	2.2	
	2.22	
	1.85	
	2.2	
	2.2	
	2.2	
	2.0	

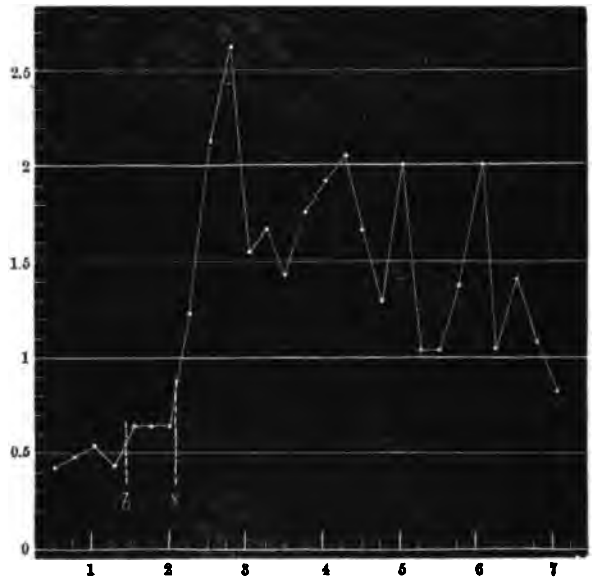
TABLE I.—*Composition of Bile before and after "Sanguinarin."*

Experiment 3.	Before.	After.
Water	90.09	91.41
Bile-acids, pigments, cholesterin, fats ...	7.38	6.57
Mucus	1.04	0.90
Ash	1.49	1.12
	100.00	100.00
Velocity of secretion per half-hour	2.4 cc.	4.25 cc.

It appears from this analysis that under the influence of "sanguinarin" the bile becomes more watery, nevertheless the velocity of secretion having been nearly doubled by this agent, it is evident that the liver secreted more biliary matter.

Experiment 4. Dog that had fasted 17 hours. Weight 20 kilogrammes. (Fig. 4.)

Fig. 4.



Secretion of bile before and after "sanguinarin." 2 cc. bile and 3 cc. water injected into the duodenum at *b*. 1 grain "sanguinarin" in the same fluid injected at *s*.

AUTOPSY.—Vascularity of the mucous membrane of upper half of small intestine somewhat increased. Considerable evidence of purgative action in upper half of small intestine. Contents of a viscid mucous character.

Results of Experiments with "Sanguinarin."—1. In one experiment three grains, in another experiment one grain, of "sanguinarin" when mixed with a small quantity of bile and water and placed in the duodenum powerfully stimulated the

liver. 2. It rendered the bile more watery, nevertheless it caused the liver to secrete more biliary matter in a given time. 3. The secretion of the intestinal glands was slightly increased by these doses. These results show that the statements of Tully and Mothershead ought not to be treated with indifference and neglect, as they at present appear to be, in practical medicine.

ACTION OF "IRIDIN."

The root of the Iris Versicolor, or American Blue Flag, is said by Wood and Bache (*lib. cit.* p. 487) to possess cathartic, emetic and diuretic properties. The American "Eclectics" have used, under the name of "iridin" or irisin, an oleo-resin obtained by precipitating a tincture of the root with water and mixing the precipitate with an equal weight of some absorbent powder. The dose of this is 1—5 grains as a purgative. "It is thought to unite cholagogue and diuretic with aperient properties" (Wood and Bache, *loc. cit.*). An anonymous writer in the *Lancet* (August 30, 1872) states that "it is gentler in its action than podophyllin, and more reliable when a slight cholagogue action is required for a lengthened period." This statement however has been generally neglected, and the substance appears to be unknown to most persons.

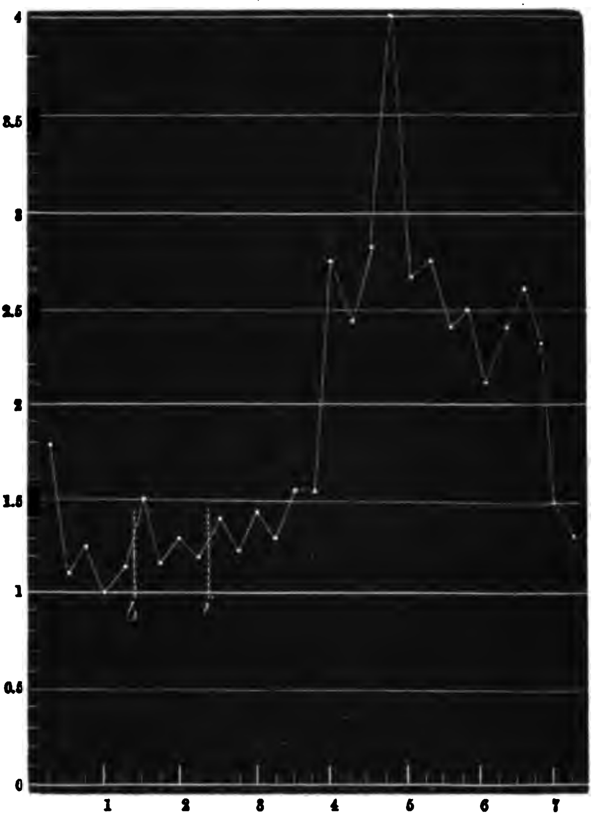
The substance employed by us is a resin prepared in the same way as euonymin (see p. 62).

Experiment 5. Dog that had fasted 17 hours. Weight 22.7 kilogrammes. (Fig. 5.)

AUTOPSY.—Stomach normal. Mucous membrane of upper two-thirds of small intestine rather more vascular than usual. This portion of the intestine contained 63 cc. of fluid, thus affording evidence of a decided purgative effect.

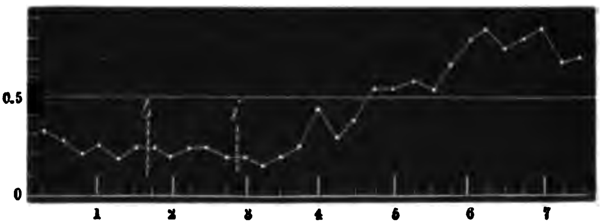
Experiment 6. Dog that had fasted 18 hours. Weight 5.4 kilogrammes. (Fig. 6.)

Fig. 5.



Secretion of bile before and after "iridin." 2 cc. bile and 3 cc. water injected into the duodenum at *b*. 5 grains "iridin" in the same fluid injected at *i*.

Fig. 6.



Secretion of bile before and after "iridin." 2 cc. bile and 2 cc. water injected into the duodenum at *b*. 5 grains "iridin" in the same fluid injected at *i*.

Experiment 4.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.41	
	0.49	
	0.52	
	0.45	
b	—	
	0.65	0.12 cc.
	0.65	
	0.65	
i	—	
	1.25	
	2.15	
	2.65	0.401 cc.
	1.55	
	1.7	
	1.45	
	1.8	
	1.9	
	2.02	
	1.7	
	1.3	
	2.0	
	1.05	
	1.05	
	1.35	
	2.0	
	1.05	
	1.4	
	1.1	
	0.8	

Experiment 5.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.8	
	1.1	
	1.25	
	1.0	
	1.15	
b	—	
	1.5	
	1.16	0.227 cc.
	1.3	
	1.2	
i	—	
	1.4	
	1.25	
	1.45	
	1.3	
	1.55	
	1.55	
	2.75	
	2.45	
	2.8	
	4.0	0.537 cc.
	2.65	
	2.75	
	2.4	
	2.5	
	2.1	
	2.4	
	2.6	
	2.3	
	1.5	
	1.3	

Experiment 6.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.32	
	0.3	
	0.2	
	0.25	
	0.2	
	0.25	
b	—	
	0.25	
	0.2	
	0.25	0.166 cc.
	0.25	
	0.2	
i	—	
	0.2	
	0.15	
	0.2	
	0.25	
	0.45	
	0.3	
	0.4	
	0.55	
	0.55	
	0.6	
	0.55	
	0.7	
	0.85	
	0.9	
	0.8	0.638 cc.
	0.85	
	0.9	
	0.7	
	0.75	

AUTOPSY.—Stomach normal. There was increased vascularity of the mucous membrane of nearly the whole length of the small intestine. The redness was not very marked, but it was greater than in the previous experiment. There was decided purgation, the small intestine containing 87 cc. of fluid with abundant mucous flocculi.

Results of Experiments with Iridin.—1. Five grains of iridin when mixed with a little bile and water and placed in the duodenum very powerfully stimulated the liver. It is not so powerful as large doses (four grains) of "podophyllin," but it is more powerful than "euonymin," as is shown by the

amount of bile secreted per kilogramme of dog; the fractions for the two "euonymin" experiments being 0.4789 cc. and 0.4678 cc., whereas in the "iridin" experiments they are 0.537 cc. and 0.638 cc. The high fraction in the second iridin experiment probably resulted from a much smaller dog getting the same dose as in the first experiment, the smaller liver being thereby stimulated to do a proportionally greater amount of work[1]. 2. Iridin is also a decided stimulant of the intestinal glands. Judging from these experiments its irritant effects on the intestinal mucous membrane are decidedly less than those of "podophyllin," while the purgative effects are greater than in the case of "euonymin." The statement of the writer in the *Lancet* (above quoted) that in man "it is gentler in its action than podophyllin" is fully supported by these experiments, and there seems every reason why this substance should be removed from its present obscurity and placed in a prominent position in practical medicine.

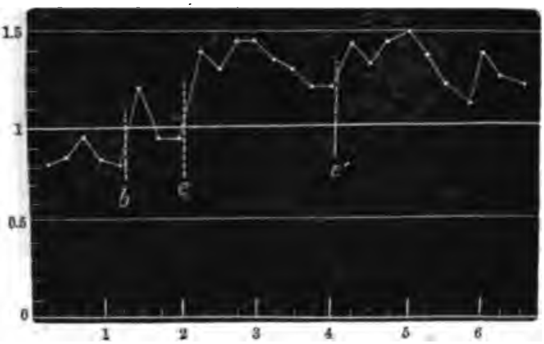
Action of "Leptandria."

"Leptandria" or "Leptandrin" is a resin prepared from the root of the American plant Leptandra Virginica or Veronica Virginica in the same manner as euonymin (see p. 62). It is a remedy that has been much lauded by the "Eclectics" as a cholagogue and tonic. As this remedy is now a good deal employed, it seemed desirable to obtain more precise information regarding its mode of action. The dose for a man is ½—3 grains three or four times daily.

Experiment 7. Dog that had fasted 18 hours. Weight 20.4 kilogrammes. (Fig. 7.)

[1] The analyses of the bile secreted before and after "iridin" were lost.

Fig. 7.



Secretion of bile before and after "leptandria." 8 cc. bile and 8 cc. water injected into the duodenum at *b*. 6 grains "leptandria" in the same fluid injected at *e*. 12 grains "leptandria" in 2 cc. rectified spirit[1] and 8 cc. water injected at *e'*.

TABLE II.—*Composition of the Bile before and after "Leptandria."*

Experiment 7.	Before.	After.
Water	91.34	91.41
Bile-acids, pigments, cholesterin, fats ...	6.64	6.60
Mucus	0.95	0.92
Ash	1.07	1.07
	100.00	100.00
Velocity of secretion per half-hour	1.9 cc.	2.5 cc.

It appears from this analysis that the bile secreted under the influence of leptandria retained its normal composition.

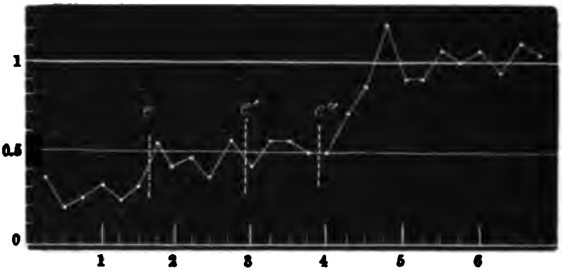
Experiment 8. Dog that had fasted 18 hours. Weight 13.1 kilogrammes. (Fig. 8.)

AUTOPSY.—Slightly increased vascularity of the mucous membrane of the upper half of the small intestine. There was slight purgation;—the upper half of the small intestine containing 37 cc. of a viscous fluid.

Results of Experiments with "Leptandria."—1. "Leptandria" when mixed with bile and placed in the duodenum undoubtedly

[1] We have ascertained that alcohol does not increase the secretion of bile, but rather diminishes it if the dose be large.

Fig. 8.



6 grains "leptandria" in 4 cc. water injected into the duodenum at *e*. $1\frac{1}{2}$ cc. bile and 3 cc. water injected at *e'*. 12 grains "leptandria" in the same fluid injected at *e''*.

stimulates the liver, but its power is very feeble as shown by the small secretion of bile per kilogramme of dog notwithstanding the large doses given. It excites the liver to secrete bile, having the ordinary composition. Unless the biliary solvent be present, "leptandria" produces scarcely any appreciable effect. In this respect it resembles many other resinous substances, e.g. "podophyllin." 2. It is a feeble stimulant of the intestinal glands.

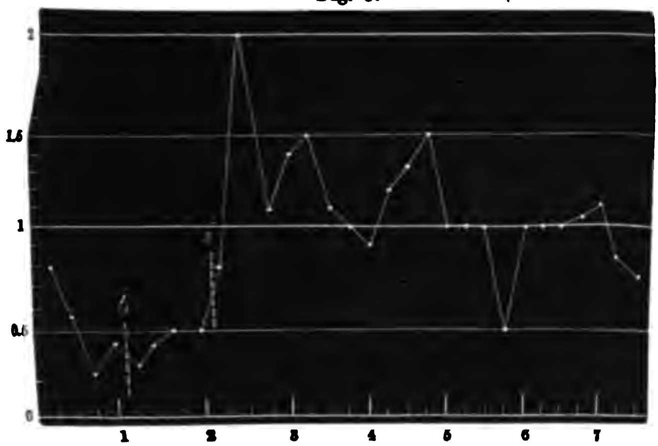
ACTION OF IPECACUAN.

As is well known, ipecacuan is regarded as almost a specific remedy in certain cases of dysentery. It is stated that it gives rise to evacuations containing a large quantity of bile. The manner in which it does this is not definitely known: some maintaining that it permits of biliary discharge by relieving spasm of the bile-ducts. The following experiments, undertaken at the desire of Sir Robert Christison, prove beyond a doubt that this substance is a powerful stimulant of the hepatic secreting apparatus.

Experiment 9. Dog that had fasted 18 hours. Weight 15 kilogrammes. (Fig. 9.)

AUTOPSY.—The ipecacuan had extended along the upper half of the small intestine, the mucous membrane of which portion was covered with thick white mucus. No purgation.

Fig. 9.



Secretion of bile before and after ipecacuan. 2 cc. bile and 3 cc. water injected into the duodenum at *b*. 60 grains ipecacuan powder in the same fluid injected at *i*.

Experiment 7.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.8	
	0.85	
	0.95	
	0.85	
	0.8	
b	—	
	1.2	0.191 cc.
	0.95	
	0.95	
e	—	
	1.4	
	1.3	
	1.45	
	1.45	
	1.35	0.272 cc.
	1.3	
	1.2	
	1.2	
e′	—	
	1.45	
	1.3	
	1.45	
	1.5	0.274 cc.
	1.35	
	1.2	
	1.1	
	1.4	
	1.25	
	1.2	

Experiment 8.

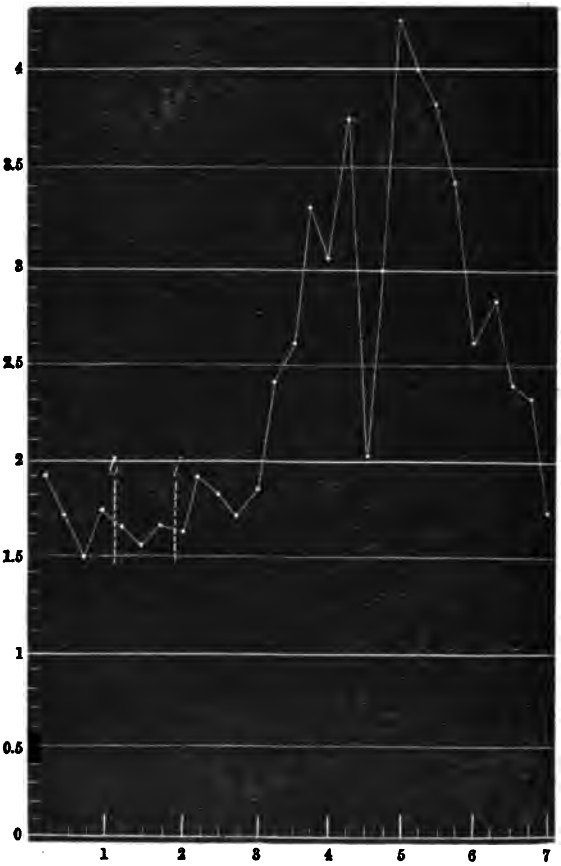
	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.35	
	0.2	
	0.25	
	0.3	
	0.25	0.0839 cc.
	0.3	
e	—	
	0.55	
	0.4	
	0.45	
	0.35	
	0.55	
e′	—	
	0.4	
	0.55	
	0.55	
	0.5	
e″	—	
	0.5	
	0.7	
	0.85	
	1.2	
	0.9	
	0.9	
	1.05	
	1.0	
	1.05	
	0.95	
	1.1	0.3167 cc.
	1.05	

Experiment 9.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.8	
	0.55	
	0.25	
	0.4	
b	—	
	0.3	
	0.4	
	0.5	0.118 cc.
	0.5	
i	—	
	0.8	
	2.0	
	1.1	
	1.4	0.4 cc.
	1.5	
	1.1	
	1.0	
	0.9	
	1.2	
	1.3	
	1.5	
	1.0	
	1.0	
	1.0	
	0.5	
	1.0	
	1.0	
	1.0	
	1.05	
	1.1	
	0.8	
	0.7	

Experiment 10. Dog that had fasted 18 hours. Weight 27.2 kilogrammes. (Fig. 10.)

Fig. 10.



Secretion of bile before and after ipecacuan. 2 cc. bile and 5 cc. water injected into the duodenum at *b*. The same fluid with 60 grains ipecacuan powder injected at *i*.

Autopsy.—Stomach normal. The ipecacuan extended along the upper two-thirds of the small intestine, the mucous membrane of which exhibited a slight increase of vascularity, and was covered with thick mucus, but there was no purgation.

Even in much smaller doses, however, ipecacuan excites the liver, as is shown by the two following experiments.

Experiment 11. Dog that had fasted 18 hours. Weight 6.1 kilogrammes. (Fig. 11.)

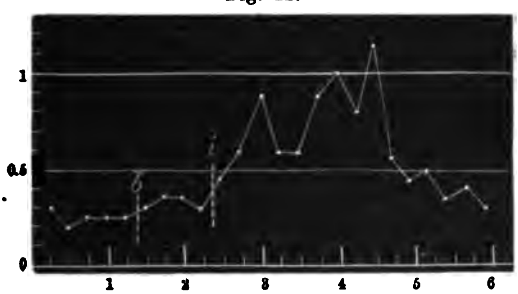
Fig. 11.

Secretion of bile before and after ipecacuan. 1.5 cc. bile and 2 cc. water injected into the duodenum at *b*. The same fluid with 3 grains of ipecacuan powder injected at *i*.

AUTOPSY.—Thick mucus covering the mucous membrane of upper fourth of small intestine. No purgation.

Experiment 12. Dog that had fasted 17 hours. Weight 6.8 kilogrammes. (Fig. 12.)

Fig. 12.



Secretion of bile before and after ipecacuan. 1.5 cc. bile and 2 cc. water injected into duodenum at *b*. 3 grains ipecacuan powder in the same fluid injected at *i*.

AUTOPSY.—The appearances of the intestine were similar to those observed in the preceding experiment.

Results of Experiments with Ipecacuan.—1. Sixty grains of powdered ipecacuan mixed with a small quantity of bile and placed in the duodenum powerfully stimulated the liver. Even three grains had an effect on a dog weighing 6.8 kilogrammes very nearly as great as the effect of sixty grains on a dog weighing 27.2 kilogrammes; the amount of bile secreted

Experiment 10.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.9	
	1.7	
	1.5	
	1.7	
b	—	
	1.65	0.24 cc.
	1.55	
	1.65	
i	—	
	1.6	
	1.9	
	1.8	
	1.7	
	1.85	
	2.4	
	2.6	
	3.3	
	3.05	
	3.75	
	2.02	
	3.0	
	4.25	0.555 cc.
	4.0	
	3.85	
	3.42	
	2.6	
	2.8	
	2.35	
	2.3	
	1.7	

Experiment 11.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.2	
	0.2	
	0.2	
	0.25	
	0.3	
	0.25	
	0.3	
	0.3	
	0.2	
b	—	
	0.25	
	0.25	0.18 cc.
	0.3	
	0.3	
i	—	
	0.4	
	0.25	
	0.3	
	0.7	
	0.7	0.385 cc.
	0.45	
	0.5	
	0.7	
	0.7	
	0.35	
	0.45	
	0.5	
	0.45	
	0.4	

Experiment 12.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.3	
	0.2	
	0.25	
	0.25	
	0.25	
b	—	
	0.3	
	0.35	0.186 cc.
	0.32	
	0.3	
i	—	
	0.45	
	0.6	
	0.9	
	0.6	
	0.6	
	0.9	
	1.0	0.506 cc.
	0.8	
	1.15	
	0.55	
	0.45	
	0.5	
	0.35	
	0.4	
	0.3	

Composition of the Bile before and after Ipecacuan.

TABLE III.

Experiment 10.	Before.	After.
Water	89.631	89.77
Bile-acids, pigments, cholesterin, fats ...	8.13	8.129
Mucus	1.01	0.87
Ash	1.229	1.231
	100.000	100.000
Velocity of secretion per half-hour	3.2 cc.	6.35 cc.

TABLE IV.

Experiment 12.	Before.	After.
Water	91.32	91.51
Bile-acids, pigments, cholesterin, fats	6.73	6.73
Mucus	0.98	0.79
Ash	0.97	0.97
	100.00	100.00
Velocity of secretion per half-hour	0.65 cc.	1.9 cc.

These analyses show that, notwithstanding the acceleration of secretion by ipecacuan, the percentage amount of the special biliary constituents remains unchanged.

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per kilogramme of dog being nearly the same in both cases. 2. The bile secreted under its influence was of normal composition as regards the biliary matter proper. 3. No purgative effect was produced, but there was an increased secretion of mucus in the small intestine. The composition of the bile did not afford any evidence of an increased secretion of mucus having taken place from the glands of the bile-ducts.

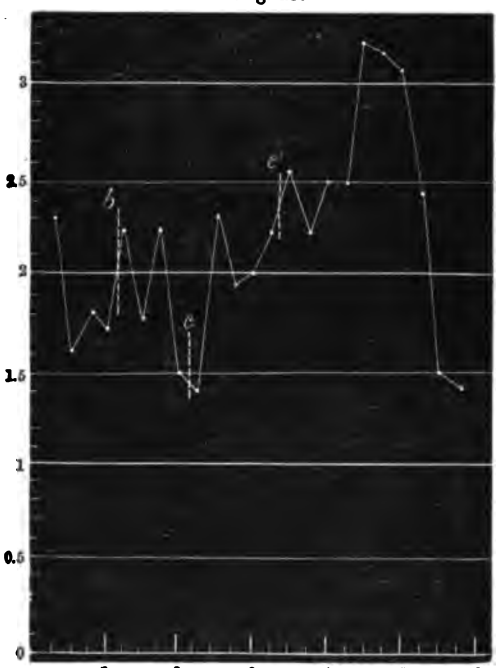
The increased biliary flow that followed ipecacuan could not in these experiments be ascribed to any relaxation of "spasm of the bile-ducts," for that no such thing existed was clearly shown by the free flow of the bile before the substance was given. Nor could it be owing to contraction of the gall-bladder, for the cystic duct was clamped. Nor can it be ascribed to contraction of the bile-ducts, for the increased flow was far too prolonged to be attributable to any such cause. It is therefore certain that this substance, like the others, has the power of stimulating the *secreting* apparatus of the liver. This being now proved as regards the dog, it can scarcely be doubted that the *modus operandi* is the same in man. The results of these experiments will therefore lead to new speculations regarding the pathology of dysentery; for *every step towards greater accuracy of knowledge regarding the* modus operandi *of any therapeutic agent is certainly calculated to advance our knowledge of the true nature of the pathological condition that is relieved or cured by it.*

ACTION OF COLOCYNTH.

Colocynth and jalap are substances whose action on the biliary secretion of the dog has already been investigated by Röhrig (*Stricker's Jahrbücher*, 1873, p. 240). According to that observer croton oil is a powerful cholagogue, and colocynth and jalap stand near it in importance. We have already pointed out the faultiness of Röhrig's method, and have shown (this *Journal*, Vol. x. p. 259) that croton oil is scarcely worthy of being classed amongst cholagogues. It seemed therefore desirable that we should experiment with colocynth and jalap in order to have results comparable with our experiments on other substances.

Experiment 13. Dog that had fasted 16 hours. Weight 26.3 kilogrammes. (Fig. 13.)

Fig. 13.

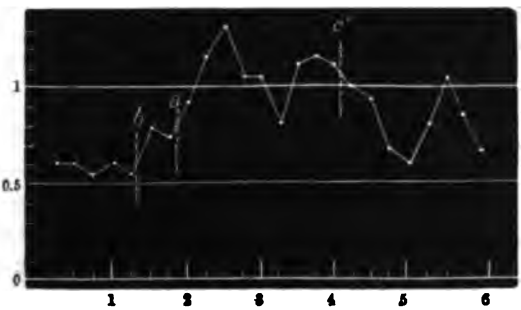


Secretion of bile before and after colocynth. 2 cc. bile and 2 cc. water injected into the duodenum at *b*. The same fluid with 7 grains of powdered colocynth pulp injected at *c*. The same dose repeated at *c'*.

AUTOPSY.—Gastric mucous membrane very vascular. The mucous membrane of the small intestine was intensely vascular throughout its entire length. There was evidence of powerful purgation,—the small intestine containing 82 cc. of fluid.

Experiment 14. Dog that had fasted 16 hours. Weight 16.3 kilogrammes. (Fig. 14.)

Fig. 14.



Secretion of bile before and after colocynth. 3 cc. bile and 3 cc. water injected into the duodenum at *c*. The same repeated at *c'*.

AUTOPSY.—There was increased vascularity throughout the whole length of the mucous membrane of the small intestine, especially marked in the upper part. There was considerable evidence of purgation.

Composition of the Bile before and after Colocynth.

TABLE V.

Experiment 13.	Before.	After.
Water	92.99	94.18
Bile-acids, pigments, cholesterin, fats ...	5.49	4.70
Mucus	0.90	0.70
Ash	0.62	0.47
	100.00	100.00
Velocity of secretion per half-hour	3.4 cc.	6.35 cc.

TABLE VI.

Experiment 14.	Before.	After.
Water	91.48	91.72
Bile-acids, pigments, cholesterin, fats ...	6.85	6.69
Mucus	0.83	0.77
Ash	0.84	0.82
	100.00	100.00
Velocity of secretion per half-hour	1.15 cc.	2.35 cc.

These analyses show that colocynth renders the bile more watery, although it at the same time increases the secretion of the special biliary matters.

In No. 13, the pulse became very weak towards the close of the experiment, and it may be that this weakness rendered the effect of the colocynth upon the liver less than it otherwise might have been. Be this as it may, we did not think it necessary to perform another experiment, for the first experiment with this substance may be regarded as sufficient.

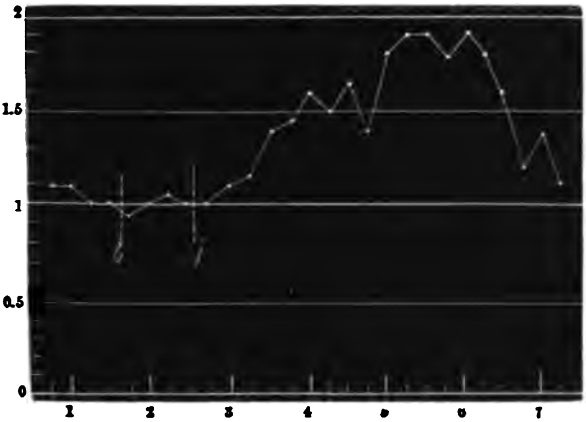
Results of the Experiments with Colocynth.—1. Colocynth is a hepatic stimulant of considerable power. It renders the bile more watery but nevertheless increases the secretion of biliary matter. 2. It is also a powerful stimulant of the intestinal glands.

ACTION OF JALAP.

Experiment 15. Dog that had fasted 17 hours. Weight 25 kilogrammes. (Fig. 15.)

AUTOPSY.—The jalap had extended along about four-fifths of the small intestine, the mucous membrane of which was more vascular than usual, especially so at the lower part of the duodenum. The purgative effect was considerable—there being 64 cc. of fluid in the intestine. The fluid was of a very watery character.

Fig. 15.



Secretion of bile before and after jalap. 2.5 cc. bile and 2.5 cc. water injected into the duodenum at *b*. 30 grains of jalap powder in the same fluid injected at *j*.

Experiment 13.

Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
cc.	
2.3	
1.6	
1.8	
b —	
1.7	
2.2	
1.75	
2.2	0.2908 cc.
1.5	
c —	
1.4	
2.3	
1.95	
2.0	
2.2	
c′ —	
2.55	
2.2	
2.5	
2.5	
3.2	
3.15	0.452 cc.
3.05	
2.45	
1.5	
1.4	

Experiment 14.

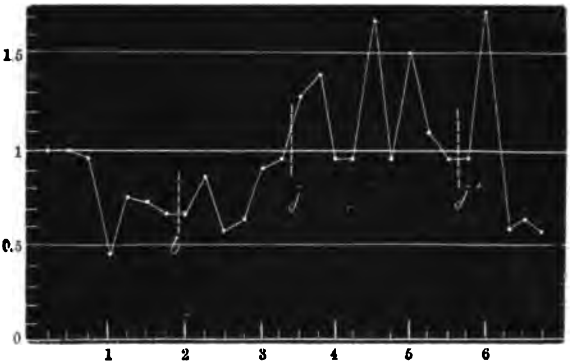
Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
cc.	
0.6	
0.6	
0.55	
0.6	
0.55	
b —	0.165 cc.
0.8	
0.75	
c —	
0.9	
1.15	
1.3	0.279 cc.
1.05	
1.05	
0.8	
1.1	
1.15	
1.1	
c′ —	
1.0	
0.95	
0.65	
0.6	
0.8	
1.05	
0.85	
0.65	

Experiment 15.

Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
cc.	
1.1	
1.1	
1.0	
1.0	
b —	
0.95	
1.0	
1.05	0.16 cc.
1.0	
j —	
1.0	
1.1	
1.15	
1.4	
1.45	
1.6	
1.5	
1.65	
1.4	
1.8	
1.9	
1.9	
1.8	
1.9	0.296 cc.
1.8	
1.6	
1.2	
1.4	
1.1	

Experiment 16. Dog that had fasted 20 hours. Weight 11.8 kilogrammes. (Fig. 16.)

Fig. 16.



Secretion of bile before and after jalap. 3 cc. water and 2 cc. bile injected into the duodenum. 20 grains jalap powder in the same fluid injected at *j*, and again at *j'*.

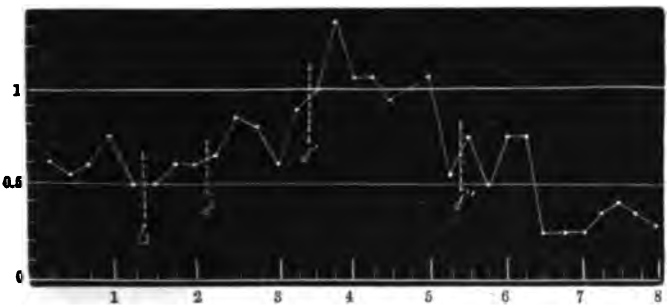
AUTOPSY.—Profuse purgative action throughout the whole extent of intestine. Vascularity of mucous membrane of small intestine somewhat increased, most marked in the duodenum.

The rapid fall in the bile secretion towards the close of this experiment probably resulted from the purgation. It is to be noted that in *Exp.* 16, a *larger* dose of jalap was given (40 grains) to a dog less than half the size of the subject of *Exp.* 15. This is doubtless the cause of the greater effect on the liver and on the intestinal glands in *Exp.* 16. The effect of a still larger dose in a dog of nearly the same weight as No. 16 is instructive. (See Fig. 17.)

Experiment 17. Dog that had fasted 22 hours. Weight 12.3 kilogrammes. (Fig. 17.)

AUTOPSY. 20 cc. of fluid had been injected into the duodenum, much of which had probably been absorbed; the small intestine, however, contained in its upper third 117 cc. of watery fluid, showing that a profuse purgative action was taking place. The jalap had extended along only a third of the small intestine.

Fig. 17.



Secretion of bile before and after jalap. 2 cc. bile and 3 cc. water injected into duodenum at *b*. 20 grains jalap powder in the same fluid injected at *j*, *j′*, and *j″*.

The fall of the bile secretion towards the close of the experiment is only another illustration of the fact often witnessed by us—*that severe purgation diminishes the secretion of bile.*

Composition of the Bile before and after Jalap.

TABLE VII.

Experiment 15.	Before.	After.
Water	89.31	89.75
Bile-acids, pigments, cholesterin, fats ...	8.41	8.05
Mucus	0.93	0.87
Ash	1.35	1.33
	100.00	100.00
Velocity of secretion per half-hour	2.1 cc.	3.7 cc.

TABLE VIII.

Experiment 16.	Before.	After.
Water	87.91	88.19
Bile-acids, pigments, cholesterin, fats ...	9.94	9.87
Mucus	0.73	0.52
Ash	1.42	1.42
	100.00	100.00
Velocity of secretion per half-hour	1.4 cc.	2.55 cc.

Experiment 16.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.0	
	1.0	
	0.95	
	0.45	
	0.75	
	0.7	
	0.65	
b	—	
	0.65	
	0.85	
	0.55	
	0.6	
	0.9	0.254 cc.
	0.95	
j	—	
	1.25	
	1.35	
	0.95	
	0.95	
	1.65	
	0.95	
	1.5	0.436 cc.
	1.05	
	0.95	
j′	—	
	0.95	
	1.75	
	0.55	
	0.6	
	0.55	

Experiment 17.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.6	
	0.55	
	0.6	
	0.75	
	0.5	
b	—	
	0.5	0.178 cc.
	0.6	
	0.6	
j	—	
	0.65	
	0.85	
	0.8	
	0.6	
	0.9	
j′	—	
	1.0	
	1.35	
	1.05	0.357 cc.
	1.05	
	0.95	
	1.0	
	1.05	
	0.55	
j″	—	
	0.75	
	0.5	
	0.75	
	0.75	
	0.25	
	0.25	
	0.25	
	0.35	
	0.4	
	0.35	0.113 cc.
	0.3	

Results of Experiments with Jalap.—1. Jalap is a hepatic stimulant of considerable power. It renders the bile more watery, but at the same time increases the secretion of biliary matter. 2. Its effect on the liver is however far less notable than its effects on the intestinal glands. Its hydrogogue cathartic effects on these were fully manifested in these experiments.

(*To be continued.*)

REMARKS ON THE ANATOMY OF THE ARMS OF THE CRINOIDS[1]. Part II. By P. HERBERT CARPENTER, B.A., *of Trinity College, Cambridge.*

DURING the last few months, a considerable number of papers have been published, relating to the Anatomy of the Crinoids[2]; and many new facts have been brought to light, more especially with regard to the "heart" of Johannes Müller and Greeff, the "centrodorsal vesicle" of Dr Carpenter. Of the four observers who have recently studied it, no two are in exact accordance as to its anatomy and relations; but they all agree as to its being enveloped in a yellowish fibrillar mass, from the ventral portion of which are given off five large radiating cords.

Each of these cords (as was shown long ago by Dr Carpenter[3]) originally passes upwards and outwards, through the canal in the centre of its corresponding interradially placed basal, in the interior of which it subdivides into two branches; and this arrangement persists in the adult, in which the separate basals are replaced by the "rosette," which is the product of their metamorphosis.

These pairs of branches enter two adjacent orifices, on the internal faces of the several contiguous pairs of first radials, between which the salient angle of each basal originally projected. Thus, each first radial receives cords from two basals; and the two adjacent cords of each pair of contiguous radials are connected by lateral commissural bands; the whole system constituting what is regarded by Dr Carpenter as a sort of circular commissure. After giving off their lateral branches for the lodgement of the commissural bands, the two canals contained in every first radial coalesce into one towards its distal border; and this single canal is continued as far as the third or axillary radial, in which it divaricates into the two brachial canals.

Dr Carpenter's account of this arrangement has recently been confirmed by Ludwig (9), who has further shown that the

[1] Read in Section D at the Glasgow meeting of the British Association, September, 1876.

[2] A list of these is given at the end of this Communication.

[3] *Phil. Trans.* 1866, pp. 714, 738, Plate XLII.

two cords which separately enter the first radials remain distinct beyond the circular commissure, and run side by side in the single canal, until they reach the third radials or axillaries, where they interchange fibres by means of a chiasma and of a simple commissure; so that the axial cord of each of the arms borne by the axillary radial receives two sets of fibres from the central mass enveloping the centrodorsal vesicle.

This fact, which I have recently been able to verify, is of considerable importance in its bearing on Dr Carpenter's views, as to the nervous character of this fibrillar envelope, and of the axial cords of the arms which proceed from it. Dr Carpenter's recent experiments at the Zoological Station at Naples (5) support his previously expressed views so very strongly, that both Ludwig, who at first (3) denied them altogether, and Greeff, seem from their latest publications (8, 9) to have tacitly accepted them. Teuscher (6), who seems to have been unacquainted with the recent investigations of other observers, appears to have arrived at the conclusion that the axial cords are nerves, by a sort of process of exclusion, but he comments on the morphological difficulties which this view seems to him to involve[1].

The axial cords proceeding from the envelope of the centrodorsal vesicle were regarded by Müller as hollow, and as communicating with its cavity. Dr Carpenter, however, describes them as solid (2, 5); and he is followed by Teuscher (6) and Ludwig (9), who have been unable to discover any definite canals in their interior. Greeff, on the other hand, spoke of them at first (1) as enclosing radial vessels; which form, if I understand him rightly, a closed blood-vascular system in connection with the heart, but he admits his inability to follow them far beyond the radial axillaries. In his second paper (8), however, in which he seems to admit the nervous character of

[1] Ludwig, apparently misled by my remarks (4) as to the morphological difficulties presented by the existence in the Crinoids of two nervous systems, a dorsal and a ventral, attributes to me (9) a doubt as to the existence of an oral nervous ring. So far, however, is this from being the case, that I was acquainted with the ventral nerve and nerve-vessel in the peristomial area of both *Antedon Eschrichtii*, and *Actinometra nigra*, as long ago as last December, some time before the appearance of any papers upon the subject; although from want of material I was unable satisfactorily to demonstrate the existence of an entire nervous ring, of which I have since been able to satisfy myself completely.

the axial cords, he states that he has been able to inject the "heart" and the vessels proceeding from it, far out into the arms, but that he is not sure whether the vessels are in the interior, or on the exterior of the axial cords.

The view that these cords are nerves is strongly supported by the very remarkable and regular manner, in which these cords give off branches in the centre of each segment of the arms and pinnules. I have already (4) described these branches in *Actinometra*, and have found them also in three species of *Antedon*, *A. rosaceus*, *A. celticus*, and *A. Eschrichtii*, though they are far less developed than in *Actinometra*; this is probably due to the fact that in *Actinometra*, at any rate in the species which I have examined, there is a pair of muscles between every two successive pinnule segments, while these pinnule muscles are absent in *Antedon*; for Dr Carpenter has shown (2) that branches which come off from the axial cords of the arms are distributed upon the ends of the muscular bundles connecting their successive segments. None of the German observers seem to be acquainted with these branches, for they make no mention of them.

Further, if the axial cords are not nerves, and the ventral bands are to be regarded as the only nervous structures in the whole Crinoid organization, the difficulty presents itself, that the oral pinnules of the European Crinoids, and more than half the arms, with the majority of the pinnules, of some forms of *Actinometra*, are entirely devoid of a nervous supply.

The oral pinnules of *Antedon* have been shown by Dr Carpenter (2) to be extremely susceptible of irritation; when they are touched in the living animal, the whole circlet of arms is suddenly and simultaneously coiled up over the disc: while irritation of one of the ordinary pinnules is simply followed by flexion of the arm which bears it.

The structure of these oral pinnules, which are borne in *Antedon rosaceus* by the second brachials, differs very considerably from that of the pinnules borne by the other brachial segments: for not only are they sterile, but they have neither tentacular apparatus nor ambulacral groove; their ventral surface being slightly convex, instead of being concave, as in the ordinary arms and pinnules. This has been mentioned by

Teuscher (6), but he has omitted to state that the ordinary ciliated epithelium of the ambulacral groove, with its subjacent nervous layer and nerve-vessel, are also absent.

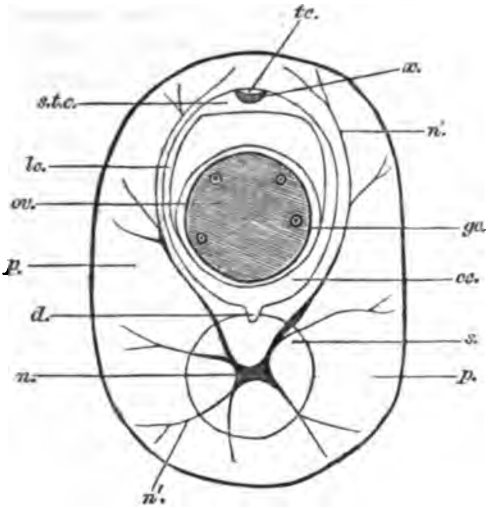
This condition, which is limited in *Antedon rosaceus* to the oral pinnules, sometimes exists in whole arms, and in all the pinnules borne by them, in *Actinometra armata;* and also in other species of the same genus, in which the mouth is excentric, and the anus central or subcentral. From the peristomial area radiate the ambulacral grooves of the ventral surface of the disc and arms; and those arms which come off from the oral side of the disc, always have distinct ambulacral grooves on their ventral surface, with a well-developed tentacular apparatus.

These grooves, however, do not—as in the European species—give off regular branches to the pinnules borne by the third and the immediately following brachial segments: but a variable number of these first pinnules, sometimes only three or four, sometimes as many as forty, resemble, in this respect, the oral pinnules; their ventral surface being convex, without any ciliated epithelium, nervous band, or nerve-vessel; and their tentacular canal (water-vessel) being simple, without any lateral extensions to respiratory leaves and tentacles.

In correspondence with this suppression of the ordinary respiratory apparatus, the subtentacular and cœliac canals, which are more directly connected with the body-cavity than the tentacular canal, seem to take on a respiratory character; for they are connected, some four or five times in each segment, by large lateral canals (*lc.* Fig. 1), which lie between the perisome of the side of the pinnule, and the large genital canal with its contained ovary or testis; thus increasing the aerating surface to which the chylopoietic fluid, mixed with the sea water that finds its way into the body-cavity through the numerous ciliated funnels on the ventral surface of the disc, is exposed.

In these oral arms, however, branches of the ambulacral groove enter the pinnules sooner or later; so that the terminal ones are always provided with a distinct tentacular apparatus. But the case is usually very different with some of the arms which come off from the aboral side of the disc; one or more of them having no groove whatever, and being itself, with all

Fig. 1.



Transverse section of a non-tentaculiferous pinnule of *Actinometra armata*. Diagrammatic[1].

tc. Tentacular canal, or water-vessel.
x. Pigmented cellular thickening of its floor.
stc. Subtentacular canal.
lc. Lateral canal connecting the subtentacular canal with
cc. Cœliac canal.
d. Ciliated diverticulum of the cœliac canal.
gc. Genital canal; only separated from the cœliac canal by a thin partition and containing
ov. Ovary.
p. Connective and other tissues of perisome.
s. Organic basis of skeleton.
n. Axial cord: or nerve.
n'. Its branches, lost in epidermic structures.

its pinnules, entirely devoid both of ventral nerve and of tentacular apparatus. The proportion of these non-tentaculiferous arms varies greatly in different individuals. In the ten-armed *Actinometra solaris*, I have met with individuals in which all the arms were normal and tentaculiferous; and others in which four out of the ten were non-tentaculiferous. In the nine specimens of *A. armata* brought by Professor

[1] This figure is made up from four *successive* sections: the nerve-branches and lateral canals run so obliquely to the long axis of the pinnule, that they are not seen throughout their whole length in any single transverse section.

Semper from the Philippines, in which the total number of arms varies from 13 to 39, I have found the proportion to vary from $\frac{3}{13}$ and $\frac{4}{20}$ to $\frac{17}{26}$ and $\frac{18}{31}$: while in one varietal form all the 33 arms were of the ordinary character; and in the three specimens of *A. fimbriata* which I have examined, all the 23 or 24 arms were normal and tentaculiferous.

Even on the disc, the difference between the oral and the aboral grooves is obvious to the unassisted eye: and my sections through the latter have shown me, that when the arms supplied by these grooves have no tentacular apparatus, that apparatus and the ventral nerve are entirely wanting in the corresponding grooves of the disc. Near the mouth, these non-tentaculiferous grooves are fairly distinct, although they are by no means so deep as the ordinary grooves, and have no respiratory leaves; but as they approach the margin of the disc they become flattened out, and are usually entirely obliterated in the arms after the first few brachial segments. In some cases, however, the groove extends some way into the arms, and gives off branches to the pinnules; but it has no epithelial and nervous floor, and its walls contain branches, not of the tentacular, but of the subtentacular canal, which thus would seem, as in the pinnules, to take on a more definite respiratory function.

Another difference between these two types of arms is that the curious problematical "sense-organs" which I have mentioned in a former paper (4), are limited to the terminal pinnules of the non-tentaculiferous arms. The three last segments of these pinnules are very small, but the centre of the dorsal surface of each of the next seven or ten segments is occupied by one of these curious bodies, which when viewed from the exterior appears as a rounded brownish mass[1].

It will be evident from what has been said above, that in some species (e.g. *A. armata*, and *A. solaris*) of the genus *Actinometra*, two very distinct types of arms may exist: the ventral surface of the one having a distinct ambulacral groove, lined by a ciliated epithelium, underneath which lie the ventral

[1] An account of the histological character of these organs, as to the function of which I am almost completely in the dark, will appear in my paper on the anatomy of this interesting species.

nerve and nerve-vessel, and being provided with a relatively large tentacular canal, which sends off alternating branches to the respiratory leaves and tentacular apparatus, borne by the walls of the groove; while in the other type of arm there is either no groove, or only a very shallow one, and neither ciliated epithelium, ventral nerve, nerve-vessel, nor tentacular apparatus. It is exclusively in the terminal pinnules of this latter type of arm, that the above-mentioned doubtful "sense-organs" occur. Occasionally, though not often, this distinction is so marked, that of the two arms borne upon the same tertiary (brachial) axillary segment, one may be tentaculiferous *with* a ventral nerve, and the other non-tentaculiferous *without* a ventral nerve: more usually, however, the passage from the one type to the other is marked by the interval between the secondary (palmar) or primary (distichal) axillaries.

Fig. 1. represents the arrangement of the organs in one of the ordinary non-tentaculiferous pinnules of *Actinometra armata.* The distribution of the branches *n'* of the axial cord (nerve) is extremely variable, and never the same on the two sides of the same pinnule, or in two successive segments; but they all come off from four main trunks, two dorsal and two ventral, and eventually lose themselves in epidermic structures. The arrangement of the lateral canals, too, is very variable; and the two ventral nerve-trunks may either run round them, as represented in the figure, or pass between two successive canals of the same segment: these trunks occasionally exhibit small swellings, either at the points at which they are about to divide or in other parts of their course.

There is one other point in the anatomy of the arms of *Actinometra armata,* to which I desire to call attention. In *Antedon,* in which the mouth is central, and the interradial areas of the ventral surface of the disc nearly equally developed, the ciliated funnels leading from the exterior into the perivisceral cavity are distributed with tolerable regularity in these areas. In *A. armata,* however, and probably in the other species of the genus, in which the mouth is pushed to one side by the great development of that interradial area in which the anus lies, the funnels are practically limited to the margin of the disc, and the central or anal area is almost or

quite destitute of them; though they are very abundant between the subdivisions of the main ambulacral grooves, proceeding from the peristomial area. They also extend out into the arms as far as the sixth brachial segment, which is usually the first to bear a genital pinnule: here however they do not lead, as might naturally be expected from their relations in the disc, into the subtentacular canal, but into the genital canal; though as this, like the subtentacular and cœliac canals, is in direct communication with the body-cavity, the analogy between these funnels, taken as a whole, and the madreporic canals of the other Echinoderms, is not disturbed in any great degree. In *Antedon*, these funnels of the disc lead into a system of sinuses, described by Dr Carpenter (2) as "left by the incomplete adhesion of the peritoneum covering the upper surface of the visceral mass, to the parietal layer which lines the under surface of the oral perisome:" they are thus parts of the cœlom, but are described (I believe erroneously) by Teuscher (6), as in connection laterally, with the subtentacular canals of the disc; his figures, however, do not show this connection, and it is not mentioned by either Grimm[1], Greeff, Dr Carpenter, or Ludwig.

Like his predecessors, Teuscher has been considerably misled by the differences between Professor Semper's figure[2] of a section of an arm of *A. armata*, and the appearances presented by a section of an arm of *Antedon rosaceus;* and in an endeavour to explain these differences, he has recourse to the hypothesis, that the ovaries figured by Professor Semper were really the subtentacular canals, into which ova had accidentally found their way. That this hypothesis is an unnecessary one will be evident from my previous paper (4): the ovaries in *Actinometra armata* really do extend into the arms, and are there connected with the rachis, as described by Professor Semper, though Teuscher seems to doubt it: and the subtentacular canal is single, not double as supposed by Teuscher, and is the one figured as *tc* by Professor Semper. The subtentacular canals are called by Teuscher the lateral

[1] *Bulletins de l'Acad. Impér. de St Pétersb.* 1872, pp. 3—8.
[2] "Kurze anatomische Bemerkungen über Comatula." *Arbeiten aus dem Zool. Zoot. Institut in Würzburg.* Band I., 1874, p. 259.

vessels, and the cœliac canal the muscular vessel; and he appears to be unacquainted with the nomenclature proposed ten years ago by Dr Carpenter, and since adopted by Ludwig.

In the course of the next few months I hope to be in a position to publish a complete account of the anatomy and systematic position of *Actinometra armata*, in the *Arbeiten aus dem Zool. Zoot. Institut in Würzburg*.

I subjoin an account of the recent literature of the subject, and beg to return my best thanks to those gentlemen who have favoured me with copies of their papers.

1. R. Greef. Ueber den Bau der Crinoideen. *Sitzungsberichte d. Ges. z. Bef. d. ges. Natw. zu Marburg*. No. 1. Jan. 13, 1876. pp. 16—29.

2. W. B. Carpenter. On the Structure, Physiology, and Development of Antedon rosaceus. *Proceedings of the Royal Society*. No. 166. Jan. 20, 1876. pp. 211—231, pl. 8, 9.

3. H. Ludwig. Beiträge zur Anatomie der Crinoideen. Nachrichten von der *Königl. Gesellschaft der Wissenschaften, und der G. A. Universität zu Göttingen*. No. 5. Feb. 23, 1876. pp. 105—114.

4. P. Herbert Carpenter. Remarks on the Anatomy of the Arms of the Crinoids. Part I. *Journal of Anatomy and Physiology*. Vol. x. April, 1876. pp. 571—585.

5. W. B. Carpenter. Supplemental note to the above paper. *Proceedings, R. S.* No. 169. 1876. pp. 1—4.

6. R. Teuscher. Beiträge zur Anatomie der Echinodermen. I. Comatula mediterranea. *Jenaische Zeitschrift*. Bd. x. pp. 243—260. Taf. VII.

7. A. Götte. Vergleichende Entwickelungsgeschichte der Comatula mediterranea. *Arch. f. microsc. Anat.* Bd. XII. 1876. pp. 583—648. Taf. XXV.—XXVIII.

8. R. Greeff. Ueber das Herz der Crinoideen. *Marburg Sitzungsberichte*. No. 5. May 18, 1876. pp. 88—95.

9. H. Ludwig. Beiträge zur Anatomie der Crinoideen. II. *Göttinger Nachrichten*. No. 13. June 28, 1876. pp. 1—9.

ON THE STRUCTURE OF THE RETINA. By J. C. EWART, M.B., *University College, London*, AND G. THIN, M.D., *London*. (Pl. III.)

THE following is an abstract of a paper sent to the Editors of this Journal, in which we endeavoured to connect the results of our observations with those of observers during the last few years. We refer especially to the memoirs of Landolt, Krause, Golgi and Manfredi, and Schwalbe, and also to the views of Heinrich Müller, Kölliker, and Max Schultze. Further, in consideration of the number of new points raised and the divergence of some of our views from those generally taught, we deemed it advisable to explain in detail the methods employed during the investigation. The result of this was that, notwithstanding our attempt to be concise, the paper assumed such dimensions that the Editors returned it with a request that it should be shortened. To meet their desire we have omitted all reference to technical details and methods, and stated our conclusions with as much brevity as is consistent with clearness, and have almost entirely abstained from allusions to other writers. This we have done with great regret.

Our position in regard to other investigators will become evident if our remarks are read in connection with the resumé given by Schwalbe in his valuable article on the retina in the Handbuch lately published under the editorship of von Graefe and Saemisch.

To fellow-workers we will gladly communicate any information desired concerning the methods employed, or regarding any matter briefly touched on in the text.

The nomenclature used throughout this paper is from within outwards, as follows; 1. Membrana limitans interna. 2. Layer of optic nerve fibres. 3. Layer of Ganglion cells. 4. Molecular layer. 5. Internal granule layer. 6. Intergranule layer. 7. External granule layer. 8. Membrana limitans externa. 9. Bacillary layer. 10. Layer of pigment epithelium.

Before examining these layers it will be well to begin with a description of the radial fibres (*Radial-fasern* of H. Müller).

In the frog's retina, these when examined in glycerine after staining the whole retina in a solution of purpurine, appeared, in the first place, as flattened cylindrical bands faintly fibrillated on their surface, with even contoured borders, and one or more nuclei adhering to them at different points. These correspond to the radial fibre figured by Schwalbe. In the

next place they may be seen, as described by Müller and Kölliker, to consist of well-defined fibres generally enclosing nuclei as they pass through the internal granule layer. On careful examination the fine fibre of Müller and Kölliker may be often found enveloped by the flattened cylindrical band of Schwalbe, Figs. 2 and 3. Hence this band forms a loose investing sheath for the true fibre. The extent to which the fibre is enveloped by membranous substance depends on the mode of preparation and produces a great variety of appearances. Frequently the fibre has been quite freed from membrane except at the inner end. When this is the case the remnant of membrane left forms the well-known trumpet-shaped end of a fibre (*Radialfaserkegel*) described and figured by Schwalbe and Müller.

The nucleus of the fibre, Fig. 2 *b*, is apt to be mistaken for nuclei lying on, but not in, the fibre. It lies in a lozenge-shaped swelling, and is best seen in purpurine preparations stained with log-wood. Differing from the narrow elliptical nucleus in the fibre are other nuclei adhering to the membranous sheath of the fibre. These nuclei are either large and oval, and correspond to one of the so-called granules, Fig. 3 *e*; or are small and round, and belong to elongated cells lying on the membrane, one of which from a purpurine preparation is figured at 1 *d*.

Differing from the authorities already referred to, we have found the true radial fibres of the frog's retina extending beyond the external limiting membrane, to the outer segments of the rods.

We will now describe the different layers.

The membrana limitans interna.—This Kölliker considers an independent membrane: but Schwalbe and Schultze believe it to be "a piece of the hyaloid membrane to which radial fibres have adhered." In papers previously published by one of us[1], the membrana limitans interna is described as distinct from the hyaloid and as covered with a layer of epithelial cells. Of the existence of this membrane and its layer of cells we have obtained further evidence during the present investigation. Fig. 8 shows part of an extensive layer of cells from the retina of a sheep preserved in carbolized serum. The cells,

[1] *Journal of Anatomy and Physiology*, May and November, 1874.

mostly hexagonal, were seen, on regulating the focus, to form a double layer over a considerable part of the surface, and under them the optic nerve and ganglionic cells were distinctly seen. The difference between these hexagonal cells and the silver markings that indicate the ends of the radial fibres is well brought out by comparing Fig. 8 with Fig. 9.

In the frog we have demonstrated the cells and the membrane on which they lie both with gold and osmic acid, and we have seen external to the membrane the network of blood-vessels. The hexagonal form of the cells is imperfectly shewn in Fig. 6, a silver preparation in which the intercellular substance alone is stained. Immediately external to this layer of cells, we find in silver preparations, the fields indicated in Fig. 7, the so-called terminal swellings of the radial fibres. When a perfectly macerated fibre is examined, the main stem is seen to split up into minute terminal fibres as soon as it becomes internal to the molecular layer; and when these fibres are completely invested by a membranous expansion, we have formed the trumpet-shaped structure (*Faser-kegel*) already referred to and indicated in Fig. 7. Besides the fibres, and the membranous investment, which may be more or less complete, a varying number of nuclei are found, the position of which is indicated in Figs. 3 and 4. From the regularity of the fields in the frog's retina, and from the position of some of the nuclei across the mouth of the trumpet-shaped expansion, Fig. 4 *b*, we might infer that the spaces correspond to a layer of cells. It is different, however, in the sheep's retina, in which the irregular fields evidently do not correspond to cell-outlines, but to the subdivisions and anastomoses of the radial fibres in a membranous substance from which the cells have disappeared. In the sheep's retina the silver lines indicated at Fig. 9 are arranged after a plan that we have not seen noticed. The surface is seen to be divided by dark parallel lines equidistant from each other, and the fields in one division never cross the line into another.

In our remarks on the layer of *optic nerve-fibres* we pass over the consideration of that part of it undoubtedly nervous in its nature: and only notice what we believe to be, most probably, connective tissue.

In our preparations we found delicate fibrillary bundles, the fibrils of which had no varicosities, were very slightly stained, and had no characteristic nervous structure. We also found among the fibrillary bundles an abundant reticulum of colourless delicate fibres, contrasting markedly with these.

In addition, we observed many elongated narrow cells applied to the surface of the smaller bundles. These were found to be of a fixed and definite type; but their number varied in different preparations, Fig. 11. Indeed from the large number of nuclei seen, we feel sure that only a small proportion of these cells was shown. We may finally say, on this point, that nuclei of a larger size were also seen, most probably nuclei of cells differing from those already described. By our present modes of preparation we are unable to determine whether these cells completely invest the bundles or not. They may, however, be identical with those cells occasionally found, in teased preparations, adhering to the inner ends of the radial fibres.

Ganglionic cell-layer.—In regard to this layer we have nothing new to add to what has been already observed.

Molecular layer.—Both on the external and internal surfaces of this layer we found small round cells investing it like an epithelium. Those investing the inner surface have a round nucleus with only a small amount of cell-matter, Fig. 12, while those covering the outer have a larger nucleus and a moderate amount of cell-substance, Fig. 13.

The ground-substance of this layer was found to be made up of a number of parallel cylindrical elements of uniform size, and with a diameter equal to that of a human red blood-corpuscle. Amongst these elements nuclei could be detected, Figs. 15 and 16. Lying on these cylinders and investing them, we detected cellular elements: but whether these were cells or only cell-nuclei, we have not as yet been able to decide. They are, however, almost exact counterparts of the cells already described by us as investing the primary fibres of the lens[1].

In vertical sections we found in the frog a division into seven or eight layers, separated from each other by clear spaces, Fig. 5. In one very successful preparation where the mole-

[1] Vide this *Journal*, Vol. x. p. 226, woodcut III.

cular layer with its outer investing cells was isolated, we noticed a decided longitudinal grooving.

Internal granule-layer.—We may regard this layer as made up of small rounded cells, arranged like an epithelium; of radial fibres with their nuclei; of small spindle cells and of narrow flat cells, sometimes adhering to the membranous substance connecting the radial fibres. The flat cells, Fig. 18, we have been able to observe in the frog, *in situ*, in at least three layers, parallel to the surface of the retina. In these cases the radial fibres have been dissolved, so that the cells are seen in their natural position. We have also noticed these cells entangled in the delicate fibrils given off from the radial fibres.

The spindle cells mentioned, Fig. 19, most probably lie in a direction perpendicular to the retina, as when isolated by teasing they are generally parallel to the radial fibres. We have been unable to distinguish the bipolar ganglionic cells of Schultze and Schwalbe. What they describe as such are most probably referable either to the spindle cells or entangled flat cells we have already spoken of.

Intergranule-layer.—The existence of flattened cells in this layer of the retina of several fishes is well known. In the frog we have found numerous large flat oval nuclei, lying parallel to the surface of the retina, Fig. 21, and sometimes arranged in a double layer. With gold and formic acid[1] we have isolated a membranous substance on which the nuclei probably lie. To this membranous substance portions of what we shall presently describe as the rod-pedicles often remain attached, Fig. 21. Besides the membrane and nuclei, which probably are closely related to it, in osmic acid preparations long macerated in glycerine, numerous delicate true fibres are found in this layer. Many of them are in direct continuity with the radial fibres. The main stem of the radial fibre passes through at right angles, but as it enters gives off a number of minute branches, which ramify in this layer. We believe that all the fibres in this layer have their origin from the radial fibres; thus agreeing with Schultze and Landolt.

In a frog's retina, treated with gold and then macerated for

[1] The method employed was essentially that described by Löwit in the *Wien. Akad. Sitz.-Bericht*, LXXI. Band.

eight days in formic acid, the external limiting membrane and the intergranule-layer were seen in section as even homogeneous vitreous looking bands. This appearance is indicated in Fig. 20. The evenness of the margins of these bands, together with the fact that they were neither composed of cells nor fibres, indicates the existence of true membranes. Further, the homogeneous band occupying the position of the intergranule-layer had like the other a double border—one border in intimate contact with the external and the other with the internal granule-layer. Hence, on the above facts, and on what is known to exist in fishes, we base the following hypothesis: namely, that in the frog the intergranule-layer consists of two cellular membranes, which bound or invest the granule layers. This agrees in the main with the ideas expounded by Krause. The appearance of flat cells with processes interspersed in a network, described by Rivolta in the retina of the horse, is probably due to the reagents employed, and cannot be held as irreconcilable with the idea of a continuous layer of cells.

External granule-layer.—This we shall describe as made up of fibres, membranes, cells, and ground-substance. In some preparations the fibres and intercellular substance are alone left, forming the substratum of the *Korn* or granule. We shall, however, not employ these terms, but consider the appearance described by them as made up of membranes, nuclei, and ground-substance. These we shall now consider in detail.

The inner segment of a rod is separated by a narrow line from the base of a small conical mass. The apex of this latter, projecting inwards, is fine and pointed, and is connected with the apex of a somewhat similar cone, whose base is adjacent to the intergranule-layer. These two we shall term respectively the outer and inner pedicles of the rods. Fig. 14.

Nearer the intergranule-layer, and in the elliptical space between adjacent outer and inner rod-pedicles, there lie elliptical bodies, pointed at both extremities, the pedicles of the cones. The outer pedicles of the rods and the cone-pedicles stain very faintly with strong log-wood. In the same preparation some of the pedicles seem to be formed of a granular matter which stains decidedly with log-wood. From a careful comparison of these, it can be seen that the tinted granular

appearance does not belong to the substance proper of the pedicle, but to an investing membrane.

In preparations by ordinary methods, nuclei form a very prominent feature in this layer in the frog's retina; these are of two kinds, viz. one round or slightly oval, the other elongated, narrow, and elliptical. The rounded ones are the nuclei of cells, which lie in two parallel rows between the external limiting membrane and the intergranular layer. Fig. 22. *b*, *c*. In the same way the elliptical nuclei are the nuclei of cells, lying in like double rows between the same limits.

In one preparation the narrow elongated nuclei could be seen to lie on the finely granular substance which encloses the rod and cone-pedicles. Fig. 22. *a*. Especially in potash preparations[1] could they be seen acting as investing cells to these rod and cone-pedicles. The *Kolben*, described by Landolt as arising from the intergranule-layer in the salamander, we believe to be one of the narrow elongated cells just described.

In preparations of the retina, well macerated in glycerine, the radial fibres may be seen to unite after passing through the layer: or to bifurcate after piercing the external limiting membrane. Thus a figure somewhat like a stirrup is formed with its concavity or convexity turned outwards according to the method of formation. When the latter is the case a single fibre may proceed out from the convexity. Fig. 25.

Such of these stirrups as are formed on the outer side of the intergranule-layer form the basis of a framework for the lodgment of the cone and inner rod-pedicles. The stirrup, with its single fibre passing outwards, is therefore not a cone bifurcating, but is due to the union of radial fibres. There is no actual continuity between the radial fibres and the rods and cones, as the radial fibres lie within funnel-shaped membranes enclosing the *Körner* or pedicles. The reversed stirrups enclose the outer rod-pedicle.

All the fibres observed by us in this layer belong to the system of radial fibres. The membranes we have spoken of are seen as small films in osmic acid preparations.

[1] For details of the method see a paper on Hyaline Cartilage in the *Quarterly Journ. for Mic. Science*, January, 1876. The fresh eye is placed entire in the solution.

The external limiting membrane.—The external limiting membrane is generally described as being formed by the terminal expansion of the radial fibres. That there are fibres in it which are indistinguishable from radial fibres can be well seen in vertical sections. But besides these and the true membranous substance shown in Fig. 20. *a*, there is a continuous layer of cells in this membrane, between which nothing visible passes from without inwards except branches of the radial fibres, and portions of thin membranes connected with them. This layer of cells may be demonstrated in the frog and toad by means of purpurine and gold, and in teased preparations the cells may be seen attached to the inner ends of the inner segments of the rods.

These cells must be distinguished from the rounded nuclei of the external granular layer, often seen projecting from the inner border of isolated rods. Such nuclei are often cut across by a line apparently indicating the position of the external limiting membrane. The difference between the two nuclei is seen by a reference to Fig. 28 *b*, in which both are indicated. Further, we believe we have demonstrated these cells in the sheep's retina by means of silver and vitreous humour preparations. A vitreous humour preparation is represented in Fig. 29. In the same preparation, by slight movements of the cover-glass, the cells could be isolated and examined free in the fluid, and their position in several instances shown by some of the inner segments of the rods remaining adherent to the surface of the small isolated patches of cells.

There is no continuity between the inner segments of the rods and cones and their corresponding pedicles (*Körner*), the cells we have described completely isolating the one from the other.

The bacillary layer.—The rods of the frog's retina are divided by histologists into two segments, an outer and inner. Between these two segments we have found a round nucleated cell completely separating the one from the other. These cells can be distinguished from the *linsenförmige Körper* of Max Schultze in osmic acid and potash preparations, Figs. 30 and 31. Sometimes in potash preparations a number of the outer segments separate in a mass from the rest of the retina with a complete layer of cells attached to their inner ends. Fig. 32.

Lying at the outer end of the inner segment is the appearance described as the lens-shaped body (*linsenförmige Körper*). This body, like the outer segment, stains in osmic acid and logwood a dark bluish colour, and contrasts strongly with the rest of the inner segment, which remains almost unstained. In potash preparations the lens-shaped body is seen forming a distinct short and almost square middle segment quite as completely divided from the inner as the outer segment. It is homogeneous in structure, and resembles closely the substance of the outer segment, and like it differs from the rest of the inner segment by being more resistent.

Looked at one way, the inner segment is of an equal breadth throughout, but when it rolls over it appears as a double concave narrow band. The oval space left between the concave margins of adjacent inner segments is partly occupied by the inner segments of the cones.

By several methods we have succeeded in demonstrating cells lying on the inner segments of the rods. In purpurine preparations macerated in glycerine numerous nuclei and fine fibres are found in the position of the rods and cones, and in osmic acid and potash preparations the complete cells are occasionally found. These cells are long, narrow, and tapering towards the external limiting membrane. One of them is represented in Fig. 34. It resembles the "Kolben" described by Landolt in the external granule layer.

We have also seen nuclei on the outer segments of the rods, and agree with those histologists who believe the outer segments to be ensheathed by a membrane.

We have not seen the axial thread described by Ritter in the outer segments of the rods, but we have sometimes seen an artificial canal produced by the gold solution.

In the mouse and the rat the outer segments stain in osmic acid darker than the inner, but the difference is not so great as in the frog. The line of separation between the two is well marked, and large masses of the outer segments are easily detached.

There are probably also narrow cells on the inner segments of the cones of the retina of the frog and hen. Fig. 35 shows several nuclei seen on one cone while it revolved under the

cover-glass from a retina treated with nitrate of silver and examined in glycerine. An entire cell from a gold and formic acid preparation is represented in Fig. 35 *a*. The outer segments of the cones in the frog pass beyond the cells lying between the outer and inner segments of the rods, and thus must pass through the small openings left between the round cells already described.

When describing the radial fibres, we mentioned that they extended beyond the external limiting membrane. At the external limiting membrane two fibres may form an arch and enclose within it the cell of the external limiting membrane. From this arch or stirrup one or two fibres may pass outwards, forming part of the framework which supports the cells and membrane of the inner segments of the rods and cones. Other fibres pass straight through the membrane, and may then bifurcate. Figs. 25 and 27 represent these different appearances[1].

The pigment epithelium of the Retina.—This has been examined in the frog, sheep, and ox: and from a consideration of our preparations, we have come to a conclusion completely opposite to that of all previous observers. The pigment is, we believe, always external to the substance of the cell. Figs, 36, 37, and 38. The grounds for this belief are as follows.

By manipulation, the pigment may be removed as a continuous layer from one part, so that we can obtain cells free from pigment, and others covered by it. If a few pigment-granules remain, they can be seen to adhere to the surface of the cell. Indeed, by care, the pigment may be left adherent to the outer ends of the rods and cones, and the cells left free from pigment. Probably the pigment-granules are cemented to the cells by a clear viscid substance.

This hypothesis that the pigment is outside the cells, gives a better explanation to some observed facts. Thus it has been noticed sometimes that a fibre, probably a radial one, has had small beads of pigment adhering to it. This has been supposed to be a process from the choroidal hexagonal cells

[1] These fibres are left after the membranous *Kerb* of Max Schultze and the substance proper of the rods and cones have been removed by prolonged maceration in glycerine.

sent up between the rods and cones. It is more probably a radial fibre isolated, with some pigment adhering to it. The pigment therefore in the retina is contained between, not in, formed elements: in spaces lately described as lymph-spaces.

If we now consider the part of the retina extending from the pigment-epithelium to the intergranule-layer, it will be seen to consist of three well-marked divisions separated by layers of flat cells. In each of these divisions the arrangement of the ground-substance is based on the same plan. Thus if we look at the rods and cones we shall find, passing from without inwards, that the rods are well developed; but the cones not. The rods next diminish in calibre, while the cones increase. The same is the case in regard to the cone- and rod-pedicles. We therefore see that where there is a deficiency in the development of the one set of elements, there is a corresponding increase in the adjacent set.

Some have maintained that the rods and cones are nerve-elements. But in no instance has any direct continuity with undoubted nerve-elements, nor any quality distinctive of nerve-structure, either physical or chemical, been shown. Thus Max Schultze has described a supposed continuity which we have already shown to be merely due to branching of radial fibres. The continuity which W. Müller has lately advanced on the ground of a carmine-stained line passing from the external granule layer to the apparent surface of a cone, is not proved by the appearance even as described and figured by that observer himself. The existence of varicosity does not strengthen this view, as we are yet in ignorance of the exact conditions for that change.

Nerve-fibres from the ganglionic cells we have not been able to trace further than the molecular layer. This however is negative: and there is probably in the retina, though yet undiscovered, as abundant a nervous supply as has been shown in the cornea.

EXPLANATION OF THE PLATE.

When not otherwise mentioned, the figures are drawn from preparations of the retina of the frog, as seen by Hartnack's objective No. 7, eyepiece No. 3.

1. Radial fibre, with an elongated cell lying on it at *d*. Purpurine.

2. Another radial fibre enclosed by membrane. *b* nucleus of fibre, *c* intergranule layer, *d* external limiting membrane. Purpurine.

3. A fibre having nuclei *a* lying across inner end of "trumpet," others *b* in and around it. Several nuclei adhere to membranes in the internal granule layer. Purpurine.

4. Three fibres passing through intergranule-layer: two of them crossing and joining others to form fibres of rod-pedicles. *a* nuclei of external limiting membrane, *b* cell across the "trumpet" end. Osmic acid, macerated in glycerine, and stained with logwood.

5. *b* Fibrillary tissue lying along internal surface of retina, *c* nuclei on inner and outer surface of molecular layer, nuclei visible in molecular layer, *a* fibre with some of the membranous substance remaining. Spaces formed by fibrils from the stem radial fibre from which cells have fallen out are visible. Purpurine.

6. Flat cells lying on inner surface of internal limiting membrane. Under them blood-vessels with blood-corpuscles. Retina injected with silver solution.

7. Silver marking on membranous substance at inner end of radial fibres, from same preparation as No. 6.

8. Double layer of cell-outlines on internal surface of sheep's retina. *a* superficial, *b* deep layer. Carbolized serum.

9. Silver markings from apparent internal surface of sheep's retina. "Radial-fasern-Kegel" of German authors.

10. Internal surface of frog's retina. *a* layer of flat cells, *b* nerve-layer, *c* blood-corpuscles lying between the cells and optic nerve-layer. Gold.

11. Cells of internal surface. *a* as at *a* No. 10, *b* elongated narrow cells lying on the bundles of the optic nerve-layer.

12. Cells lying on internal surface of molecular layer *a*, ganglion-cells lying amongst them *b*. Gold and formic acid.

13. Layer of cells on external surface of molecular layer: between them radial fibres pass and give off fine processes which surround the cells. Osmic acid. Hartnack, objective 8, eyepiece 2.

14. Purpurine preparation macerated in glycerine: fine processes from radial fibres form a network for cells of internal granule-layer. *a* the outer and *f* the inner pedicle of a rod covered with their sheaths, *d* the outer with its complete sheath, *b* the outer with a nucleus on the sheath, *c* pedicle of cone, *g* nucleus on cone-pedicle, *h* external limiting membrane.

15. Hen's retina in glycerine, parallel to the surface of the retina. Molecular layer is seen to be made up of fine narrow parallel bands with nuclei amongst them.

16. Gold and formic acid preparation, showing narrow bands of molecular layer partly covered by elongated cells: parallel to the surface of the retina. Round nuclei are also seen at different parts.

17. Cells on outer surface of molecular layer with small spindle-cells lying amongst them parallel to surface of retina. Potash.

18. Layer of cells from internal granule-layer; (three such layers were seen above each other). Potash.

19. Spindle elements lying in the internal granule-layer.

20. Gold preparation, showing, *a* the external limiting membrane, and *b* intergranule-layer as homogeneous bands: effect of eight days maceration in formic acid.

21. Large nuclei of intergranule-layer and villus-like processes on surface, which belong to external granule-layer. Osmic acid.

22. Gold and formic acid preparation. *a* narrow cells, *b* nucleus on cone-pedicle, *c* nucleus on outer rod-pedicle, *d* lens-shaped body, *f* isolated cell, *e* similar cell from a potash preparation.

23. *a* Outer segment and *b* inner segment of rod, *c* "lens-shaped body," *d* cell of external limiting membrane, *e* the outer, *f* the inner rod-pedicle, *g* narrow cells on membrane connecting them, *h* nucleus of inter-granule layer. Osmic acid. Hartnack, objective 8, eyepiece 2.

24. *a* Nuclei in intergranule-layer, *b* nucleus on outer rod-pedicle, *c* nucleus on cone-pedicle, *d* cellular substance between outer and inner segments of rod, *e* radial fibre bifurcating as it enters intergranule-layer, *f* external limiting membrane. Osmic acid. Hartnack, objective 8, eye-piece 2.

25. Radial fibre passing outwards through external limiting membrane. *a* nucleus, *c* external limiting membrane.

26. *e* outer pedicle of rod freed from membrane by maceration, *f* fibre passing along-side of pedicle but not in direct contact with it, *c* external limiting membrane, *d* inner segment of rod.

27. Two divisions of a radial fibre converging on the sheath of a cone. *a* fibre, *b* sheath. Cone-substance has disappeared by maceration.

28. *a* Lens-shaped body, *b* nucleus of external limiting membrane, *c* nucleus on outer rod pedicle, *d* nucleus on cone-pedicle. Osmic acid and logwood.

29. Cells on external limiting membrane of sheep's retina examined in vitreous humour sixteen hours after death.

30. *a* Granular cell-substance between the segments of the rods.

31. *a* "Lens-shaped body," *b* cell-substance between segments.

32. Cells on inner ends of outer segments of rods. Potash.

33. *a* Lens-shaped body freed from membrane, *b* external limiting membrane, *c* nucleus on outer rod-pedicle. Injected with silver solution from the heart.

34. An isolated cell from surface of rods: osmic acid and glycerine maceration.

35. Nuclei seen on the same cone in different positions, assumed by its moving under the pressure of the cover-glass. *a* narrow cell from surface of cone.

36. Cells of pigment layer. *a* cells without pigment, *b* mass of pigment between cells and ends of rods, *c* pigment between rods, *e* "lens-shaped body," *f* inner segment. Potash.

37. Internal surface from pigment-layer of ox's retina. *a* pigment still covering cell, *b* partly removed, *c* pigment completely removed.

38. Section through pigment-layer. *a* cells free from pigment, *b* pigment over and around ends of rods.

39. Radial fibre dividing into fine processes which pass upwards through external granule-layer. *a* external limiting membrane, *b* outer rod-pedicle.

40. *a* Outer rod-pedicle freed from membrane, *b* inner segment of rod, *c* external limiting membrane.

SUPPLEMENTARY REMARKS "ON THE PHYSIOLOGICAL EFFECTS OF SEVERE AND PROTRACTED MUSCULAR EXERCISE, WITH ESPECIAL REFERENCE TO ITS INFLUENCE UPON THE EXCRETION OF NITROGEN." *By* AUSTIN FLINT, JUN., M.D., *Professor of Physiology in the Bellevue Hospital Medical College, New York, etc., etc.*

IN June, 1871, I published in the *New York Medical Journal* an account of a series of observations made upon Weston, the pedestrian, during one of his remarkable feats of endurance. My researches, which at that time I regarded as very important, have lately received additional interest from the fact that they have been in part repeated and confirmed in England by Dr Pavy. My original observations were made with the utmost care, and they involved a great deal of labour. They were most decidedly opposed, in their results, to the modern view regarding the influence of muscular exercise upon the excretion of urea, which is based upon the experiments of Fick and Wislicenus, made in 1866, and upon other observations apparently confirmatory of the idea that the elimination of urea is not increased by muscular work. This view I believe to be incorrect; and I regard the experiments upon which it rests as imperfect, faulty, and made under unphysiological conditions.

The question of the influence of muscular exercise upon the elimination of nitrogen being of great importance in its pathological as well as in its physiological relations, it was to be expected that conclusions opposed to the generally-accepted ideas, even when deduced from very extended experiments, would be viewed with distrust and receive adverse criticism. I have not failed to realize this expectation, although it seemed to me that my conclusions could not be successfully controverted without a denial of the accuracy or the truth of my experimental data. I shall here refer merely to the criticisms of Dr Pavy, as he is now the only physiologist who is in a position to judge, from his own knowledge, of the reliability of my observations. These criticisms, however, seem to me to be general rather than

definite and positive. They are summed up substantially in the following paragraph, quoted from Dr Pavy's work on *Food and Dietetics*:—

"Now, apart from the fact that a marked deviation from the physiological state existed when the results upon which the conclusions are based were yielded, is there anything in the results to show that in reality we have more to deal with than simply a consumption of nitrogenous material within the system beyond the supply for the time from without? Taking the figures throughout, there is not much more to be seen than a difference occasioned by a falling off in the amount of nitrogen ingested during the first four days of the walk; and it is well known that when the ingesta do not furnish what is wanted for meeting the expenditure going on (as during inanition), the resources of the body are drawn upon, and the nitrogenous matter existing in the various parts—both solids and fluids—wastes or yields itself up as well as the rest. On the fifth day, after a prolonged sleep, which appears to have restored the flagging powers, the previous relation was reversed. The food ingested afforded more than enough to meet the requirements. There was a gain of 1¾ lb. in body-weight, and according to the figures, the nitrogen discharged fell short by 50·27 grains of that which entered, notwithstanding a walk of forty miles and a half was performed[1]."

This paragraph, without a knowledge of the details of my experiments, may seem obscure. I conceive that Dr Pavy intended to reason as follows:—Although I had demonstrated, for the first four days of a walking feat performed by Mr Weston in which he had walked, the first day 80 miles, the second day 48 miles, the third day 92 miles, and the fourth day 57 miles, that there was a large increase in the nitrogen excreted over the nitrogen of food, it is assumed by Dr Pavy that this apparent excess was due to a deficient ingestion of nitrogen and not necessarily to an increase in the excretion of nitrogen. The fact is that, comparing four days, during which 277 miles were walked, with four days before, during which 26 miles were walked, we had, in four days, walking 26 miles, 1,336·06 grains of nitrogen in the food, against 790·78 grains during four days,

[1] Pavy, *Food and Dietetics*, Philadelphia, 1874, p. 71.

walking 277 miles, or a deficiency in the nitrogen of food during the latter period of 545·28 grains. During the four days, walking 26 miles, the nitrogen excreted was 1,252·17 grains, against 1,473·85 grains during the four days, walking 277 miles, or an excess of nitrogen excreted of 221·68 grains. It is thus evident that the excessive exertion of walking 277 miles in four consecutive days induced an increase in the excretion of nitrogen, not only sufficient to equal the deficiency of the nitrogen of food, but a considerable excess. The excess of the nitrogen excreted during the four days, walking 277 miles, over the four days, walking 26 miles, irrespective of the nitrogen ingested, was 221·68 grains; and the excess of nitrogen excreted during the four days, walking 277 miles, over the nitrogen ingested during the four days, walking 26 miles, was 137·79 grains. It seems to me that the figures and deductions which I gave in my original article, in which I show the effects of prolonged and severe muscular exercise upon the excretion of nitrogen, not only in absolute quantity, but in proportion to the nitrogen ingested, are sufficiently clear and distinct, and the complications in these deductions, if they exist, are due to the process of reasoning from my figures employed by Dr Pavy. It does not appear that any physiological demonstration could be more positive than that of the proposition that muscular exercise increases not only the absolute quantity of nitrogen excreted, but the proportionate quantity of nitrogen eliminated to the nitrogen of food.

My first impression, in studying the experiments of Fick and Wislicenus, was that the observations upon the influence of exercise upon the elimination of nitrogen were made upon a purely non-nitrogenized diet on account of the labour and difficulty attending an accurate estimation of the nitrogen of food; but it now seems to me that this was not the only idea with which this method of experimentation was adopted. It is a seductive, and was a more or less novel idea, that the animal organism, after it has become fully developed, is a machine which consumes food as fuel, and that it does not constantly wear out its own substance by work and repair itself by the ingesta. With this view, it would seem possible to reduce the values of food to mathematical accuracy, calculating the heat-units, foot-

pounds, etc., of various articles of diet. Such calculations would be very indefinite for any restricted period of time, if we adopted the view that the nitrogenized constituents of the body wear and are consumed with muscular work, and that they are regenerated by the nitrogenized matter of food. A necessary basis for an accurate estimation of heat and work-units of food is the idea that food is directly consumed in the production of heat and in work. While calculations of these units with mathematical accuracy would be very desirable, as giving definite form to our ideas of the value of food, they still want a positive basis in fact. In carrying out this idea, it seems to me that the value of many of the experiments is made to depend upon the assumption of the truth of the proposition which they are intended to support.

In view of the great importance of the results obtained by me, and, as I believe, confirmed by the recent observations of Dr Pavy, it would be interesting to assimilate and compare the two sets of observations, the more so as I could scarcely have hoped that independent researches would have been made under the same remarkable and unusual conditions; viz. the same subject undertaking a similar feat of endurance. In the account published by Dr Pavy thus far, I do not find any reference to the results obtained by me in 1870 and published in 1871. If I should not be anticipated by Dr Pavy, I shall be interested to place the figures of the two series of observations side by side; but I hope that Dr Pavy, who is now fully prepared to criticise my results, will give them the study and attention that he bestowed upon them when he had had no opportunity of personally testing their accuracy. In the calculations which I made of the amount of nitrogen of food, I used the same estimates for all the periods, before, during, and after the walk. If any errors existed in these estimates, such errors would have equal value in the different periods and would not materially change the comparative results. It would be interesting to use these same estimates in calculating the nitrogen of the food taken while Mr Weston was under the observation of Dr Pavy.

Corrections in the Tables published in 1871.

In calculating the proportion of nitrogen excreted to the nitrogen of food, I fell into an error sufficiently serious to demand correction, although it does not affect the general conclusions deduced from my observations. I first calculated the amount of nitrogen excreted for every hundred parts of nitrogen of food, for each day, by multiplying the nitrogen excreted by 100 and dividing by the nitrogen of food, which gave correct results; but, in calculating the average proportion of nitrogen excreted for the five days before the walk, five days of the walk, and five days after the walk, I added for each period the proportionate excretion of nitrogen for the five days, and obtained the average by dividing by five. This was an error, as I was using relative and not absolute quantities. I fell into this error simply because the process was a little easier than to divide the average amount of nitrogen excreted for the five days by the average amount of nitrogen ingested for the same period. My results from this faulty process of calculation, with the correct results, are given below:—

	First Period—Five Days before the Walk.	Second Period—Five Days of the Walk.	Third Period—Five Days after the Walk.
Nitrogen of food	339.46 grains	234.76 grains	440.98 grains
Nitrogen excreted	315.09 „	361.52 „	373.15 „
Nitrogen excreted per 100 parts of Nitrogen of food	(Incorrect) 96.53 parts	(Incorrect) 174.81 parts	(Incorrect) 91.98 parts
Nitrogen excreted per 100 parts of Nitrogen of food, obtained by the correct process	(Correct) 92.82 parts	(Correct) 158.99 parts	(Correct) 84.63 parts

I made a similar error in my calculations of the averages for each of the three periods of five days each, of the uric acid per 100 parts of urea. I append the corrected tables, the figures corrected being marked with a †.

TABLE C(1).*

Analyses of Excretions.—Urine and Fæces.

First Period—Five Days before the Walk.

(French weights within brackets.)

URINE.	1st Day, Nov. 16.	2d Day, Nov. 17.	3d Day, Nov. 18.	4th Day, Nov. 19.	5th Day, Nov. 20.	Averages.
Quantity	39.55 fl. oz. (1,170.0 c. c.)	38.08 fl. oz. (1,125.0 c. c.)	46.15 fl. oz. (1,365.0 c. c.)	32.45 fl. oz. (960.0 c. c.)	34.00 fl. oz. (1,050.0 c. c.)	37.84 fl. oz. (1,184.0 c. c.)
Specific gravity	1024.0	1024.4	1023.1	1027.6	1025.2	1024.9
Urea	650.08 grains (42.120)	590.35 grains (38.250)	658.08 grains (42.815)	607.56 grains (39.366)	640.18 grains (41.476)	628.24 grains (40.706)
Nitrogen in urea	303.37 " (19.656)	275.60 " (16.517)	304.77 " (19.747)	283.52 " (18.370)	296.73 " (19.355)	2[illegible]8.18 " (18.729)
Uric acid	3.55 " (0.230)	4.03 " (0.261)	0.94 " (0.061)	1.06 " (0.069)	1.73 " (0.112)	2.26 " (0.127)
Phosphoric acid	51.46 " (3.334)	44.08 " (2.921)	45.14 " (2.925)	67.00 " (4.341)	43.01 " (2.787)	50.14 " (3.262)
Sulphuric acid	38.37 " (2.486)	40.92 " (2.651)	38.86 " (2.518)	51.50 " (3.337)	38.18 " (2.474)	41.67 (2.698)
Chloride of sodium	195.02 " (12.636)	158.00 " (10.237)	191.70 " (12.421)	106.68 " (6.912)	145.85 " (9.450)	159.45 (10.331)
Abnormal matters	Large amount of oxalate of lime (octahedra).	Larger amount of oxalate than on Nov. 16th.	Small amount of oxalate.	Large amount of oxalate, with amorphous urates.	Large amount of oxalate.	
FÆCES.						
Quantity	3.70 oz. (105.0)	4.78 oz. (135.5)	4.76 oz. (135.0)	3.17 oz. (90.0)	3.97 oz. (112.5)	4.08 oz. (115.6)
Nitrogen in fæces	19.89 grains (1.289)	25.68 grains (1.664)	25.59 grains (1.658)	17.05 grains (1.105)	21.33 grains (1.382)	21.91 grains (1.421)
Nitrogen in urea and fæces combined	323.26 grains (20.945)	301.18 grains (18.181)	330.36 grains (21.405)	300.57 grains (19.475)	320.06 grains (20.737)	315.09 grains (20.149)
Nitrogen of urea and fæces per 100 pts. N. food	89.49	104.45	121.38†	89.72†	72.67	92.82†
Uric acid per 100 pts. of urea	0.538	0.683	0.144	0.174	0.270	0.360†

The fæces contained an average of 72 per cent. of water.

* Page 48 of Memoir, and page 654 of the "New York Medical Journal."

TABLE C(II).*

Analyses of Excretions.—Urine and Fæces.

Second Period—Five Days of the Walk.

(French weights within brackets.)

URINE.	1st Day, Nov. 21.	2d Day, Nov. 22.	3d Day, Nov. 23.	4th Day, Nov. 24.	5th Day, Nov. 25.	Averages.
Quantity	42.09 fl. oz. (1,245.0 c. c.)	33.50 fl. oz. (991.0 c. c.)	40.56 fl. oz. (1,200.0 c. c.)	32.52 fl. oz. (965.0 c. c.)	43.60 fl. oz. (1,290.0 c. c.)	38.46 fl. oz. (1,138.0 c. c.)
Specific gravity	1028.6	1030.0	1032.5	1029.6	1022.6	1028.7
Urea	710.00 grains (46.065)	702.86 grains (45.540)	851.95 grains (55.200)	688.98 grains (44.641)	657.02 grains (42.570)	722.16 grains (46.803)
Nitrogen in urea	331.33 " (21.497)	328.00 " (21.252)	397.58 " (25.760)	321.52 " (20.832)	306.61 " (19.866)	337.01 " (21.841)
Uric acid	0.32 " (0.021)	0.14 " (0.009)	4.74 " (0.307)	9.21 " (0.597)	0.57 " (0.037)	3.00 " (0.194)
Phosphoric acid	84·95 " (5.504)	72.14 " (4.674)	102.26 " (6.625)	66.30 " (4.296)	57.49 " (3.725)	76.63 " (4.965)
Sulphuric acid	73.39 " (4.755)	56.90 " (3.687)	63.71 " (4.128)	32.66 " (2.116)	40.84 " (2.646)	53.50 " (3.666)
Chloride of sodium	96.00 " (6.220)	91.68 " (5.940)	44.45 " (2.880)	28.78 " (1.865)	64.50 " (4.179)	65.08 " (4.217)
Abnormal matters	Large amount of oxalate of lime (octahedra).	Same as Nov. 21st.	Very large amount of oxalate.	Small amount of oxalate.	Small amount of oxalate, with amorphous phos.	
FÆCES.						
Quantity	4.80 oz. (136.0)	7.94 oz. (225.0)	None	5.03 oz. (142.5)	4.87 oz. (138.0)	4.53 oz. (128. 3)
Nitrogen in fæces	25.77 grains (1.670)	42.64 grains (2.763)	"	27.01 grains (1.750)	26.16 grains (1.695)	24.32 grains (1.576)
Nitrogen in urea and fæces combined	357.10 grains (22.167)	370.64 grains (24.015)	397.58 grains (25.760)	348.53 grains (22.582)	332.77 grains (21.561)	361.52 grains (23.217)
Nitrogen of urea and fæces per 100 pts. N. food	235.63	139.39	173.91	240.86	84.27	153.99†
Uric acid per 100 pts. of urea	0.045	0.020	0.556	1.336	0.087	[illegible]

TABLE C(3).*

Analyses of Excretions.—Urine and Fæces.

Third Period—Five Days after the Walk.

(French weights within brackets.)

URINE.	1st Day, Nov. 26.	2d Day, Nov. 27.	3d Day, Nov. 28.	4th Day, Nov. 29.	5th Day, Nov. 30.	Averages.
Quantity	31.59 fl. oz. (937.5 c. c.)	46.14 fl. oz. (1,365.0 c. c.)	84.18 fl. oz. (2,490.0 c. c.)	60.38 fl. oz. (1,786.0 c. c.)	68.39 fl. oz. (2,023.0 c. c.)	58.14 fl. oz. (1,720.8 c. c.)
Specific gravity	1025.8	1024.4	1019.7	1022.5	1022.6	1028.0
Urea	593.23 grain (38.437)	716.29 grains (46.410)	768.61 grains (49.800)	744.32 grains (48.226)	811.48 grains (52.598)	726.79 grains (47.094)
Nitrogen in urea	276.84 " (17.937)	334.27 " (21.658)	358.68 " (23.240)	347.35 " (22.505)	378.69 " (24.546)	339.17 " (21.977)
Uric acid	0.48 " (0.031)	0.52 " (0.034)	0.31 " (0.020)	2.51 " (0.163)	3.30 " (0.214)	1.42 " (0.092)
Phosphoric acid	29.06 " (1.883)	46.93 " (3.041)	105.68 " (6.847)	50.76 " (3.289)	52.00 " (3.364)	56.89 " (3.674)
Sulphuric acid	49.53 " (3.209)	46.07 " (2.985)	53.57 " (3.471)	48.73 " (3.157)	47.20 " (3.058)	49.02 " (3.176)
Chloride of sodium	66.41 " (4.303)	170.64 " (11.056)	622.58 " (40.338)	297.70 " (19.288)	404.65 " (26.218)	312.40 " (20.241)
Abnormal matters	Small amount of oxalate of lime (octahedra), with amorph. urates.	Trace of sugar; small amount of oxalate; uric-acid crystals.	Same as on Nov. 27.	No abnormal matters.	Moderate amount of oxalate.	
FÆCES.						
Quantity	3.51 oz. (99.5)	4.57 oz. (129.5)	9.53 oz. (270.0)	6.61 oz. (187.5)	7.41 oz. (210.0)	6.33 oz. (179.3)
Nitrogen in fæces	18.86 grains (1.222)	24.54 grains (1.590)	51.19 grains (3.316)	35.54 grains (2.303)	39.80 grains (2.579)	33.99 grains (2.202)
Nitrogen in urea and fæces combined	295.70 grains (19.159)	358.81 grains (23.248)	409.87 grains (26.556)	382.89 grains (24.808)	418.49 grains (27.125)	373.15 grains (24.179)
Nitrogen of urea and fæces per 100 pts. N. of food	76.68	71.81	103.81	59.67	147.69	84.63†
Uric acid per 100 pts. of urea	0.081	0.072	0.040	0.337	0.406	0.195†

The fæces contained an average of 72 per cent. of water.

* Page 52 of Memoir, and page 558 of the "New York Medical Journal."

TABLE D*.

Daily Averages for the Three Periods.

(French weights and measures within brackets.)

	First Period—Five Days before the Walk.	Second Period—Five Days of the Walk.	Third Period—Five Days after the Walk.
Weight	Loss in 5 days—21.8 oz. (598 gr.)	Loss in 5 days—55.2 oz. (1,565 gr.) Loss in 4 days—83.2 oz. (2,358 gr.)	Gain in 5 days—80 oz. (2,268 gr.)
	Average of 5 days—	Average of 5 days—	Average of 5 days—
Temperature	99° Fahr. (37.2° C.)	96.3° Fahr. (35.7° C.)	98.6° Fahr. (37° C.)
Pulse	78	90	74
Respirations	23	21	25
Sleep	8 h. 5 m.	3 h. 17 m.	8 h. 29 m.
Miles walked	8.2 miles	63.5 miles	2.2 miles
Ingesta	100.50 oz. (2,848.82 gr.)	171.47 oz. (4,860.57 gr.)	144.59 oz. (4,098.62 gr.)
Nitrogen of food	339.46 grains (21.994)	234.76 grains (15.211)	440.98 grains (28.569)
Cutaneous and pulmonary exhalation	61.68 oz. (1,690.91 gr.)	136.41 oz. (3,875.18 gr.)	62.82 oz. (1,706.78 gr.)
URINE.			
Quantity	37.84 fl. oz. (1,134.0 c. c.)	38.46 fl. oz. (1,138.0 c. c.)	58.14 fl. oz. (1,720.3 c. c.)
Specific gravity	1024.9	1028.7	1023.0
Urea	628.24 grains (40.706)	722.16 grains (46.808)	726.79 grains (47.094)
Nitrogen in urea	293.18 " (18.729)	337.01 " (21.841)	339.17 " (21.977)
Uric acid	2.26 " (0.127)	3.00 " (0.194)	1.42 " (0.092)
Phosphoric acid	50.14 " (3.262)	76.63 " (4.965)	56.69 " (3.674)
Sulphuric acid	41.57 " (2.693)	56.50 " (3.666)	49.02 " (3.176)
Chloride of sodium	159.45 " (10.331)	65.08 " (4.217)	312.40 " (20.241)
FÆCES.			
Quantity	4.08 oz. (115.6)	4.53 oz. (128.3)	6.33 oz. (179.3)
Nitrogen	21.91 grains (1.421)	24.32 grains (1.576)	33.99 grains (2.202)
Nitrogen in urea and fæces combined	315.09 grains (20.149)	361.52 grains (23.217)	373.16 grains (24.179)
Nitrogen of urea and fæces per 100 pts. of Nitrogen of food	92.82† parts	153.99† parts	84.63† parts
Uric acid per 100 pts. of urea	0.360† parts	0.415† parts	0.195† parts

* Page 53 of Memoir, and page 659 of the "New York Medical Journal."

THE GENERATIVE ORGANS OF THE PARASITIC ISOPODA. *By* J. F. BULLAR, B.A., *Trinity College, Cambridge.* (Pl. IV.)

IN the following pages are recorded some observations on the generative organs of some of the parasitic Isopoda. My investigations were carried on last spring in Dr Dohrn's Zoological Station, and my best thanks are due to him for his help and advice, as well as to Dr Eisig for his kind assistance during my stay at Naples.

The species investigated are the following:—

Cymothoa œstroides (Risso).
Nerocila maculata (M. Edw.).
Nerocila bivittata (Risso).
Anilocra physodes (Lin.).
Anilocra mediterranea (M. Edw.).

With the exception of the last they were kindly determined for me by Prof. Heller. They are all hermaphrodite. The generative organs are essentially alike in all. To avoid future confusion it may be well to state at once that the organs are paired, and those of the two sides quite distinct. The animals during the development of the generative products pass through three distinct stages, which may be distinguished by the following characters.

In the first stage[1] they have externally the appearance of males. There is a double penis (Pl. IV. fig. 4 P.), situated in the median line of the ventral wall of the last thoracic segment. The internal parts of the generative organs on each side consist (Pl. IV. fig. 1) of the ovary and the testes and their ducts. The ovary and testes form a continuous gland, of which the ovary is the posterior simple tubular portion, while the testes appear anteriorly as three cæcal diverticula at its outer border. The oviduct, a widish tube continuous with the wall of the ovary, arises from the outer border of the ovary behind the testes, and runs to the anterior edge of the sixth thoracic segment, where, at this stage, it ends

[1] C. œstroides and A. mediterranea are the only species which I have obtained in this stage.

blindly. The vas deferens is continued from the posterior end of the ovary; it is much narrower than the oviduct; after running straight backwards for a short distance it turns outwards and downwards, and opens externally at the extremity of the penis of its side.

Between the first and second stage a moult takes place, and the penis being part of the skin is thrown of, and in the second stage there is no penis. Neither the vas deferens nor oviduct have an external opening.

In the third stage the vas deferens still remains closed, but the oviduct has acquired a slit-like aperture at the anterior edge of the sixth thoracic segment, just at the base of the posterior flap of the brood-pouch, which is present at this stage.

I will now describe each stage more fully.

In the first stage the generative gland is always comparatively small, owing to the incompletely developed state of the ovary. This may be very small, containing only a few young ova, or it may contain more numerous ova, some of a considerable size. Except in the case of the very youngest ovaries it is easily seen that the formation of the fresh ova takes place only along the outer border of the organ (Pl. IV. fig. 2).

The testes (Pl. IV. fig. 1 T.) at this stage are fully developed; they often contain numerous spermatozoa.

The spermatozoa are arranged in bundles (Pl. IV. fig. 6) with their heads all pointing one way, and are so disposed that the anterior end of the bundle is wedge-shaped. Each spermatozoon (Pl. IV. fig. 6) consists of a very long thin filament tapering to a point at the posterior extremity. The anterior extremity is thicker, and here a peculiarly twisted leaf-like appendage is attached to it (Pl. IV. fig. 6). The spermatozoa are perfectly motionless. Their average length is 1.15 Mm., and that of the appendage .04 Mm.

The bundles of spermatozoa may be seen in the act of making their way from the testes down the outer side of the ovary to the vas deferens. They always pass downwards head foremost.

The vas deferens (Pl. IV. fig. 1 VD.) is usually filled with spermatozoa, and, except at a very early stage, presents a fusiform enlargement near its lower end, which is crowded with

spermatozoa. The outer surface of this enlargement is generally covered with branched pigment-cells.

In the second stage the skin has been changed, and, as stated above, the oviduct and vas deferens are both closed externally.

The ovary has increased considerably in size, and frequently many of the ova are completely developed. Young ova are also being formed along the outer margin of the ovary.

The wall of the ovary is an exceedingly fine membrane, lined internally with a single layer of large flattened epithelium-cells (Pl. IV. fig. 5), each of which contains generally four, but sometimes three or two conspicuous nuclei. Both the protoplasm and nuclei of the cells are very granular, the latter usually containing one or more larger granules. As the young ova increase in size they move away from the germinal part of the ovary, pushing out its wall where they come in contact with it to suit their shape, so that at this stage the wall of the ovary loses its primitive even outline. Owing to these changes each ovum, when examined with a high power, appears to be surrounded by a ring of cells, but by careful focussing, it can be easily seen that these are the lining cells of the wall of the ovary.

The oviduct is lined internally with a single layer of flattened epithelium-cells, continuous with those lining the wall of the ovary, but differing from them in being smaller and in containing only a single nucleus. The oviduct is provided with an external layer of longitudinal muscular fibres, which are continued on each side along the outer border of the ovary. There are apparently no circular fibres.

The testes have not increased in size. They contain, as before, spermatozoa.

The vas deferens is also filled with spermatozoa, the enlargement at its lower end being usually crowded with them.

At this stage the skin of the ventral surface can, with care, be separated like a blister from the body wall, and beneath it the flaps of the brood-pouch are seen arising as small oval buds from near the bases of the legs. At first they are quite soft and flat, but as they increase in size they become thrown into numerous small wrinkles, and at the same time it becomes

more and more easy to remove the outer skin. While the brood-flaps are being developed a very delicate chitinous skin is formed over the ventral surface beneath them. The brood-flaps reach their full development in size before the loose outer skin is thrown off.

The hardening of the brood-flaps by the formation of an outer chitinous layer is probably a quick process, for in individuals in which, as sometimes happens, half the outer skin is shed at a time the uncovered flaps are quite hard, while those remaining covered are still soft. Probably the hardening of the brood-flaps helps to burst the outer skin.

The young flaps are covered externally by a flattened epithelium. The chitinous layer is formed subsequently, and is quite structureless.

In the third stage, which is attained on the shedding of the outer skin, described in the last stage, the animal possesses a completely developed brood-pouch, formed by the overlapping flaps. The skin of the ventral surface is exceedingly delicate, and is now protected by the brood-pouch. The ovaries at the first part of the stage are very large, and fill nearly the whole of the body-cavity, causing the ventral wall to protrude considerably.

Very soon, however, the eggs are laid, and it is therefore a rare thing to find an individual of this stage with the eggs still in the ovary. When the eggs are laid the shape of the body is altered, the ventral wall being now pressed close up to the dorsal surface.

The testes (Pl. IV. fig. 3 T.) still remain; they have not increased in size, and look withered and dry, though they occasionally contain a few bundles of spermatozoa.

The vasa deferentia (Pl. IV. fig. 3 VD.), especially their enlargements, are still filled with spermatozoa.

The manner in which the ova are fertilised is a point which I have not as yet been able to determine satisfactorily. The oviduct only opens externally at the time when the brood-pouch is present, and as its opening is situated inside the brood-pouch it seems quite impossible that spermatozoa could be introduced into it by another animal.

There is often not more than one individual on a fish, and

as these solitary individuals may have embryos in their brood-pouches, they must either have fertilised their own ova, or be parthenogenetic, for they cannot be imagined to pass from one fish to another; indeed for one species at least, C. æstroides, which cannot swim, this is impossible.

Now self-impregnation, if it occurs, must be internal, for the vas deferens becomes closed before the eggs are laid, and remains so until after their development is complete.

Of course if self-impregnation occurs in these cases it occurs always. We have already seen that from the position of the external opening of the oviduct, the ova of one animal cannot be impregnated by another before they are laid. Therefore the only way in which we can imagine that a cross occurs is by supposing that self-fertilisation does not act until after the eggs have been laid, and that the spermatozoa of another individual are introduced by some means, at present unknown, into the brood-pouch, and have a prepotent effect.

It should be remembered that the brood-flaps overlap a great deal, and are not capable of being moved, and also that the spermatozoa are immoveable. These facts make it difficult to understand how the spermatozoa could by any possibility be introduced.

These animals show perhaps better than any others the manner in which hermaphroditism is acquired.

I think no one can doubt that all the Isopoda have descended from a common bisexual stock, and that the ancestors of the present parasitic species when they began to be parasitic were bisexual. It is evident that their hermaphroditism is the effect and not the cause of their habits. If a free form varied so as to be hermaphrodite, it would have, as far as we can see, no advantage over the bisexual forms, and would not therefore tend to be preserved. On the other hand, it is of such immense advantage to a parasitic animal to be hermaphrodite that such a variation would be almost certain to be preserved.

In the present case hermaphroditism was probably gained by the occurrence of a sport. The following considerations seem to show clearly that it was not the result of gradual modification.

The internal generative organs of the hermaphrodites re-

semble exactly the combined male and female organs of the free forms, such as Asellus aquaticus, described by G. O. Sars (*Crust. d'eau douce*). It is hardly credible that this would be the case if gradual modification either in the males or females had taken place.

The same argument applies to the external brood-pouch and penis, which are identical with those found in the free forms.

From the analogy of vertebrates it is reasonable to conclude that every embryo contains parts capable of developing into the generative organs of both sexes, and it is conceivable that from these parts both sets of organs may in certain cases become developed and functional. If we imagine such a sport to have been developed in one of the parasitic ancestors of the present animals, and to have produced some individuals like itself, it is all that is required to account for the hermaphroditism of the existing parasitic Isopoda.

DESCRIPTION OF THE FIGURES.

T. Testes. V.D. Vas deferens. S. Spermatozoa. O. Ovary. P. Penis.

Fig. I. Generative organs of A. mediterranea. First stage. The whole of the vas deferens and oviduct are not shewn.

Fig. II. Generative organs of C. æstroides. First stage. The vas deferens and one of the testes are not shewn.

Fig. III. Generative organs of A. physodes. Third stage—after the eggs have been laid.

Fig. IV. Penis and part of ventral wall of last thoracic segment of C. æstroides.

Fig. V. Cells from wall of ovary. First stage.

Fig. VI. Spermatozoa of A. mediterranea; only the anterior parts are represented.

ON THE DIGESTIVE FERMENT OF NEPENTHES.

BY SYDNEY H. VINES, B.A., B. SC., *Fellow of Christ's College, Cambridge.*

THE publication of Dr Hooker's Address at the Belfast Meeting of the British Association for the Advancement of Science (August, 1874), and of Mr Darwin's book on *Insectivorous Plants*, has given rise to several investigations into the nature of the phenomena described in those works.

In the *Botanische Zeitung* for Oct. 29, 1875, Reess and Will of Erlangen published a series of experiments upon Drosera rotundifolia. They made a glycerin extract from the leaves, just in the same way as a glycerin extract is made from the glands of animals, and found that this extract, when acidified with very dilute hydrochloric acid, exercised a distinct digestive influence, causing complete solution of shreds of swollen-up fibrin within the space of eighteen hours. They found also that the filtrate from the fluid in which the fibrin had been dissolved gave the characteristic reaction of peptone when treated with caustic potash and copper sulphate (Biuret-reaction). They further found that the glycerine extract had naturally a feebly acid reaction, but that still no digestion of fibrin occurred when dilute hydrochloric acid was not added to the extract. By these experiments they clearly demonstrated the similarity, amounting to identity, of the phenomena which occur on the surface of the leaf of Drosera to those which take place in the digestive cavity of an animal. In both it appears that a ferment is secreted by the gland-cells, which is capable, in the presence of dilute acid, of converting proteids into peptones.

Similar experiments have been made by von Gorup-Besanez[1] with reference to Nepenthes. In this case, however, the secretion itself was the subject of experiment. Shreds of fibrin, prepared according to the method of Grünhagen, were rapidly attacked when exposed to the action of the secretion at a temperature of about 40° C., and the digestion was more

[1] *Berichte der deutsch-chem, Gesellschaft zu* Berlin. Jahrg. 9, No. 9. May 22, 1876.

rapid when dilute hydrochloric acid (0·2%) had been added. The filtered fluid gave the characteristic reaction of peptones, when treated with caustic potash and copper sulphate.

Contemporaneously with von Gorup-Besanez I had entered upon an investigation of the nature of the phenomena described by Dr Hooker as occurring in the pitchers of Nepenthes.

In my experiments upon Nepenthes (hybridus and gracilis) I followed the method pursued by Reess and Will in their experiments on Drosera, that is to say I made a glycerin extract of the pitchers. After having placed a shred of swollen-up fibrin in a small quantity of the extract, to which a few drops of dilute hydrochloric acid had been added, I found that, after eight hours at a temperature of 40° C. the filtrate gave a distinct peptone reaction, although the fibrin was not completely dissolved. I had also placed a similar shred of fibrin in a test-tube containing a small quantity of the dilute acid, and another in a test-tube containing a small quantity of the glycerin extract, which, I may add, was neutral in reaction. The filtrates from the fluids contained in these two tubes gave no trace of peptone when tested with caustic potash and copper sulphate.

These experiments show that in the gland-cells of the pitchers of Nepenthes, as in those of the leaves of Drosera, there is contained a digestive ferment which resembles that existing in the peptic glands of animals, in that it is soluble in glycerin, and in that it is capable of converting proteid into peptones in the presence of a sufficient quantity of acid.

In comparing the results of my experiments on the digestive power of a glycerine extract of Nepenthes pitchers, with those obtained by von Gorup-Besanez in his experiments with the secretion itself, I was struck by the great rapidity of the digestive process in the latter case, and I inferred that the quantity of ferment present in the glycerine extract must be very much smaller than that present in the secretion. Reference to similar experiments made upon the stomachs of animals shewed that Ebstein and Grützner[1] had found that a glycerin extract of much greater digestive power could be obtained from a gastric mucous membrane which had been previously treated with

[1] *Pflüger's Archiv*, Bd. VIII. p. 122—151. 1873.

dilute hydrochloric acid, than from a perfectly fresh one. The researches of Heidenhain[1] on the digestive ferment of the pancreas shew that from this organ also a more active glycerin extract could be obtained when it had been previously treated with a dilute acid. From his own experiments on the pancreas, and from those of Ebstein and Grützner on the stomach, he infers that these digestive ferments are not at first formed as such within the gland-cells. He regards the gland-cells as secreting an inert substance, which he terms zymogen, which may perhaps be a combination of the ferment with an albuminoid. It is only when this zymogen is decomposed, as a result of post-mortem change, or by the action of acids, that the ferment is liberated.

These investigations suggested that possibly the digestive ferment of Nepenthes might also be set free as a consequence of the decomposition of an inert body analogous to zymogen. Accordingly I treated some pitchers of Nepenthes hybridus and gracilis with dilute acetic acid (1%) for twenty-four hours previously to the preparation of the glycerin extract. On comparing the glycerin extract made from the pitchers so treated, with that made from fresh pitchers (gathered at the same time from the same plants), I found that the digestive power of the former greatly exceeded that of the latter. For instance, I placed a small pellet of swollen-up fibrin in a tube containing a small quantity of the acid extract, and a similar pellet in a tube containing a small quantity of the extract from the fresh pitchers. To each tube I added two cubic centimeters of dilute HCl. (·2%) and exposed them both to a temperature of 40°C. At the end of six hours the fibrin in the former tube had undergone complete solution, whereas that in the latter had decreased only slightly in size. The filtrates of both gave peptone reaction, though much more strongly in the first case than in the second.

Briefly summarising the results to which my experiments on Nepenthes lead, I find that in the first place, they confirm those of von Gorup-Besanez, and those of Reess and Will, in the demonstration of the fact that "carnivorous" plants are capable of digesting proteid matters by a process which is essentially

[1] *Pflüger's Archiv*, Bd. x. p. 581. 1875.

similar to that by which the gastric digestion of animals is performed; and that, in the second place, they point out that the mode of origin of the digestive ferment, in Nepenthes at least, is essentially similar to that indicated by Heidenhain with reference to the digestive ferment of the pancreas (pancreatin), and by Ebstein and Grützner as regards that of the stomach (pepsin).

The foregoing is an abstract of a paper read before the Linnæan Society of London on June 15, 1876. Since that time I have more than once repeated my experiments, always with the same results. I have also followed the same line of investigation with reference to Sarracenia (flava), but I have failed, as yet, to obtain any indication of the presence of a digestive ferment in the pitchers of that plant.

I have also endeavoured to find out whether any diastatic ferment is present in the glands of these plants. In the case of Nepenthes the glycerin extract had no action upon starch, a result which von Gorup-Besanez also obtained in his experiments with the secretion.

In the case of Sarracenia I was surprised to find that a mixture of the glycerin extract with starch gave a well-marked sugar reaction. This I found to be due to the presence of sugar in the extract.

The fact that sugar occurred in the extract of Sarracenia, from which the digestive ferment was absent, as well as the fact that no sugar was found in the Nepenthes extract, in which the presence of the ferment was detected, seems to indicate that the pitchers of Sarracenia were in a condition in which their digestive function was in abeyance. Further experiments with this plant, we may hope, will shew that under other conditions the gland-cells of the plant, like those of Nepenthes, give rise to a digestive ferment.

THE DEVELOPMENT OF ELASMOBRANCH FISHES.

By F. M. BALFOUR, B.A., *Fellow of Trinity College, Cambridge.* (Plates V. and VI.)

Development of the Trunk.

Continued from Vol. X., p. 688.

BY the stage when the external gills have become conspicuous objects, the rudiments of the greater number of the important organs of the body are definitely established.

Owing to this fact the first appearance of the external gills forms a very convenient break in the Elasmobranch development; and in the present section the history is carried on to the period of this occurrence.

While the last chapter dealt for the most part with the formation of the main organic systems from the three embryonic layers, the present one has for its subject the gradual differentiation of these systems into individual organs. In treating of the development of the separate organs a divergence from the plan of the last chapter becomes necessary, and the following arrangement has been substituted for it. First of all an account is given of the development of the external epiblast, which is followed by a description of the organs derived from the mesoblast and of the notochord. The development of the head and whole nervous system will be dealt with in a succeeding chapter, and a separate chapter will be devoted both to the alimentary tract and the vascular system.

External Epiblast.

During stages G to I the epiblast[1] is formed of a single layer of flattened cells; and in this, as in the earlier stages, it deserves to be especially noticed that the epiblast is never more than *one cell deep*, and is therefore incapable of presenting any differentiation into nervous and epidermic layers. (Pl. v. fig. 1—5).

[1] Unless the contrary is stated, the facts recorded in this chapter apply only to the genera Scyllium and Pristiurus.

The cells which compose it are flattened and polygonal in outline, but more or less spindle-shaped in section. They present a strong contrast to the remaining embryonic cells of the body in possessing a considerable quantity of clear protoplasm, which in most other cells is almost entirely absent. Their granular nucleus is rounded or oval, and typically contains a single nucleolus. Frequently, however, two nucleoli are present, and when this is the case an area free from granules is to be seen around each nucleolus, and a dark line, which could probably be resolved into granules by the use of a sufficiently high magnifying power, divides the nucleus into two halves. These appearances probably indicate that nuclei, in which two nucleoli are present, are about to divide.

The epiblast cells vary in diameter from ·022 to ·026 Mm. and their nuclei from ·014 to ·018 Mm. They present a fairly uniform character over the greater part of the body. In Torpedo they present nearly the same characters as in Pristiurus and Scyllium, but are somewhat more columnar. (Pl. v. fig. 7.)

Along the summit of the back from the end of the tail to the level of the anus, or slightly beyond this, epiblast cells form a fold—the rudiment of the embryonically undivided dorsal fin—and the cells forming this, unlike the general epiblast cells, are markedly columnar; they nevertheless, here as elsewhere, form but a single layer. (Pl. v. fig. 3 and 5 *df.*) Although at this stage the dorsal fin is not continued as a fold anteriorly to the level of the anus, yet a columnar thickening or ridge of epiblast, extending along the median dorsal line nearly to the level of the heart, forms a true morphological prolongation of the fin.

On the ventral side of the tail is present a rudiment of the ventral unpaired fin, which stops short of the level of the anus, but, though less prominent, is otherwise quite similar to the dorsal fin and continuous with it round the end of the tail. At this stage the mesoblast has no share in forming either fin.

In many sections of the tail there may be seen on each side two folds of skin, which are very regular, and strongly simulate the rudimentary fins just described. The cells composing them are, however, not columnar, and the folds themselves are merely artificial products due to shrinking.

as these solitary individuals may have embryos in their brood-pouches, they must either have fertilised their own ova, or be parthenogenetic, for they cannot be imagined to pass from one fish to another; indeed for one species at least, C. œstroides, which cannot swim, this is impossible.

Now self-impregnation, if it occurs, must be internal, for the vas deferens becomes closed before the eggs are laid, and remains so until after their development is complete.

Of course if self-impregnation occurs in these cases it occurs always. We have already seen that from the position of the external opening of the oviduct, the ova of one animal cannot be impregnated by another before they are laid. Therefore the only way in which we can imagine that a cross occurs is by supposing that self-fertilisation does not act until after the eggs have been laid, and that the spermatozoa of another individual are introduced by some means, at present unknown, into the brood-pouch, and have a prepotent effect.

It should be remembered that the brood-flaps overlap a great deal, and are not capable of being moved, and also that the spermatozoa are immoveable. These facts make it difficult to understand how the spermatozoa could by any possibility be introduced.

These animals show perhaps better than any others the manner in which hermaphroditism is acquired.

I think no one can doubt that all the Isopoda have descended from a common bisexual stock, and that the ancestors of the present parasitic species when they began to be parasitic were bisexual. It is evident that their hermaphroditism is the effect and not the cause of their habits. If a free form varied so as to be hermaphrodite, it would have, as far as we can see, no advantage over the bisexual forms, and would not therefore tend to be preserved. On the other hand, it is of such immense advantage to a parasitic animal to be hermaphrodite that such a variation would be almost certain to be preserved.

In the present case hermaphroditism was probably gained by the occurrence of a sport. The following considerations seem to show clearly that it was not the result of gradual modification.

The internal generative organs of the hermaphrodites re-

semble exactly the combined male and female organs of the free forms, such as Asellus aquaticus, described by G. O. Sars (*Crust. d'eau douce*). It is hardly credible that this would be the case if gradual modification either in the males or females had taken place.

The same argument applies to the external brood-pouch and penis, which are identical with those found in the free forms.

From the analogy of vertebrates it is reasonable to conclude that every embryo contains parts capable of developing into the generative organs of both sexes, and it is conceivable that from these parts both sets of organs may in certain cases become developed and functional. If we imagine such a sport to have been developed in one of the parasitic ancestors of the present animals, and to have produced some individuals like itself, it is all that is required to account for the hermaphroditism of the existing parasitic Isopoda.

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From the analogy of vertebrates it is reasonable to conclude that every embryo contains parts capable of developing into the generative organs of both sexes, and it is conceivable that from these parts both sets of organs may in certain cases become developed and functional. If we imagine such a sport to have been developed in one of the parasitic ancestors of the present animals, and to have produced some individuals like itself, it is all that is required to account for the hermaphroditism of the existing parasitic Isopoda.

DESCRIPTION OF THE FIGURES.

T. Testes. V.D. Vas deferens. S. Spermatozoa. O. Ovary. P. Penis.

Fig. I. Generative organs of A. mediterranea. First stage. The whole of the vas deferens and oviduct are not shewn.

Fig. II. Generative organs of C. œstroides. First stage. The vas deferens and one of the testes are not shewn.

Fig. III. Generative organs of A. physodes. Third stage—after the eggs have been laid.

Fig. IV. Penis and part of ventral wall of last thoracic segment of C. œstroides.

Fig. V. Cells from wall of ovary. First stage.

Fig. VI. Spermatozoa of A. mediterranea; only the anterior parts are represented.

The development of the limbs is almost identically similar to that of the dorsal fins. There appears a lateral linear thickening of epiblast, which however does not, like the similar thickening of the fins, grow into a distinct fold. Its development becomes confined to two special points, at each of which is formed a continuous elongated fold of columnar cells precisely like the fold of skin forming the dorsal fins. These two folds form the paired pins. If it be taken into consideration that the continuous lateral fin, of which the rudiment appears in Elasmobranchs, does not exist in any adult Vertebrate, and also that a continuous dorsal fin exists in many Fishes, the small differences in development between the paired fin and the dorsal fins will be seen to be exactly those which might have been anticipated beforehand. Whereas the continuous dorsal fin, which often persists in adult fishes, attains a considerable development before vanishing, the originally continuous lateral one has only a very ephemeral existence.

While the facts of development strongly favour a view which would regard the limbs as remnants of a primitively continuous lateral fin, there is nothing in the structure of the limbs of adult Fishes which is opposed to this view. Externally they closely resemble the unpaired fins, and both their position and nervous supply appear clearly to indicate that they do not belong to one special segment of the body. They appear rather to be connected with a varying number of segments; a fact which would receive a simple explanation on the hypothesis here adopted[1].

My researches throw no light on the nature of the skeletal parts of the limb, but the suggestion which has been made by Günther[2] with reference to the limb of Ceratodus (the most primitive known), that it is a modification of a series of parallel rays, would very well suit the view here proposed.

[1] For the nervous supply in fishes, vide Stannius *Peripher. Nerv. System d. Fische*. In Osseous Fishes he states that the thoracic fin is supplied by branches from the first three though sometimes from the first four spinal nerves. In Accipenser there are branches from the first six nerves. In Spinax the limb is supplied by the rami anteriores of the fourth and succeeding ten spinal nerves. In the Rays not only do the sixteen anterior spinal nerves unite to supply the fin, but in all there are rami anteriores from thirty spinal nerves which pass to the thoracic limb.

[2] *Philosophical Transactions*, 1871.

Dr Dohrn[1] in speaking of the limbs, points out the difficulties in the way of supposing that they can have originated *de novo*, and not by the modification of some preexisting organ, and suggests that the limbs are modified gill-arches; a view similar to which has been hinted at by Professor Gegenbaur[2].

Dr Dohrn has not as yet given the grounds for his determination, so that any judgment on his views is premature.

None of my observations on Elasmobranchs lends any support to these views; but perhaps, while regarding the limbs as the remains of a continuous fin, it might be permissible to suppose that the pelvic and thoracic girdles are altered remnants of the skeletal parts of some of the gill-arches which have vanished in existing Vertebrates.

The absence of limbs in the Marsipobranchii and Amphioxus, for reasons already insisted upon by Dr Dohrn[3], cannot be used as an argument against limbs having existed in still more primitive Vertebrates.

Though it does not seem probable that a dorsal and ventral fin can have existed contemporaneously with lateral fins (at least not as continuous fins), yet, judging from such forms as the Rays, there is no reason why small balancing dorsal and caudal fins should not have coexisted with fully developed lateral fins.

Mesoblast. G—K.

The mesoblast in Stage F forms two independent lateral plates, each with a splanchnic and somatic layer, and divided, as before explained, into a vertebral portion and a parietal portion. At their peripheral edge these plates are continuous with the general mesoblastic tissue of the non-embryonic part of the blastoderm; except in the free parts of the embryo, where they are necessarily separated from the mesoblast of the yolk-sac, and form completely independent lateral masses of cells.

During the stages G and H, the two layers of which the mesoblast is composed cease to be in contact, and leave be-

[1] *Ursprung d. Wirbelthiere und Functionswechsels.*
[2] *Grundriss d. Vergleichenden Anat.* p. 494.
[3] *Loc. cit.*

tween them a space which constitutes the commencement of the body-cavity (Pl. v. fig. 1). From the very first this cavity is more or less clearly divided into two distinct parts; one of them in the vertebral portion of the plates of mesoblast, the other in the parietal. The cavity in the parietal part of the plates alone becomes the true body-cavity. It extends uninterruptedly through the anterior parts of the embryo, but does not appear in the caudal region, being there indicated only by the presence of two layers in the mesoblast plates. Though fairly wide below, it narrows dorsally before becoming continuous with the cavity in the vertebral plates. The line of junction of the vertebral and parietal plates is a little ventral to the dorsal summit of the alimentary canal (Pl. v. fig. 5). Owing to the fact that the vertebral plates are split up into a series of segments (protovertebræ), the section of the body-cavity they enclose is necessarily also divided into a series of segments, one for each protovertebra.

Thus the whole body-cavity consists of a continuous parietal space which communicates by a series of apertures with a number of separate cavities enclosed in the protovertebræ. The cavity in each of the protovertebræ is formed of a narrowed dorsal and a dilated ventral segment, the latter on the level of the dorsal aorta (Pl. v. fig. 5). Cavities are present in all the vertebral plates with the exception of a few far back in the tail; and exist in part of the caudal region posterior to that in which a cavity in the parietal plate is present.

Protovertebræ. Each protovertebra[1] or vertebral segment of the mesoblast plate forms a flattened rectangular body, ventrally continuous with the parietal plate of mesoblast. During stage G the dorsal edge of the protovertebræ is throughout on about a level with the ventral third of the spinal cord. Each vertebral plate is composed of two layers, a somatic and a splanchnic, and encloses the already-mentioned section of the body cavity. The cells of both layers of the plate are columnar, and each consists of a very large nucleus, invested by a delicate layer of protoplasm.

[1] No attempt has been made to describe in detail the different appearances presented by the protovertebræ in the various parts of the body, but in each stage a protovertebra from the dorsal region is taken as typical.

Before the end of stage H the inner or splanchnic wall of the protovertebra loses its simple constitution, owing to the middle part of it, opposite the dorsal two-thirds of the notochord, undergoing peculiar changes. These changes are indicated in transverse sections (Pl. v. fig. 5 and 6 *m p'*), by the cells in the part we are speaking of acquiring a peculiar angular appearance, and becoming one or two deep; and the meaning of the changes is at once shewn by longitudinal horizontal sections. These prove (Pl. vi. fig. 10) that the cells in this situation have become elongated in a longitudinal direction, and, in fact, form typical spindle-shaped embryonic muscle-cells, each with a large nucleus. Every muscle-cell extends for the whole length of a protovertebra, and in the present stage, or at any rate in stage I, acquires a peculiar granulation, which clearly foreshadows transverse striation (Pl. vi. fig. 11—13).

Thus by stage H a small portion of the splanchnopleure which forms the inner layer of each protovertebra, becomes differentiated into a distinct band of longitudinal striated muscles; these almost at once become functional, and produce the peculiar serpentine movements of the embryo, spoken of in a previous section, Vol. x. p. 560.

It may be well to say at once that these muscles form but a very small part of the muscles which eventually appear; which latter are developed at a very much later period from the remaining cells of the protovertebræ. The band developed at this stage appears to be a special formation, which has arisen through the action of natural selection, to enable the embryo to meet its respiratory requirements, by continually moving about, and so subjecting its body to fresh oxydizing influences; and as such affords an interesting example of an important structure acquired during and for embryonic life.

Though the cavities in the protovertebræ are at first perfectly continuous with the general body-cavity, of which indeed they merely form a specialized part, yet by the close of stage H they begin to be constricted off from the general body-cavity, and this process is continued rapidly, and completed shortly after stage I, and considerably before the commencement of stage K. (Pl. v. fig. 6 and 8). While this is taking place, part of the splanchnic layer of each protovertebra, immediately below the

muscle-band just described, begins to proliferate, and produce a number of cells, which at once grow in between the muscles and the notochord. These cells are very easily seen both in transverse and longitudinal sections, and form the commencing vertebral bodies (Pl. v. fig. 6, and Pl. vi. fig. 10 and 11 *Vr*).

At first the vertebral bodies have the same segmentation as the protovertebræ from which they sprang; that is to say, they form masses of embryonic cells separated from each other by narrow slits, continuous with the slits separating the protovertebræ. They have therefore at their first appearance a segmentation completely different from that which they eventually acquire (Pl. vi. fig. 11).

After the separation of the vertebral bodies from the protovertebræ, the remaining parts of the protovertebræ may be called muscle-plates; since they become directly converted into the whole voluntary muscular system of the trunk. At the time when the cavity of the muscle-plates has become completely separate from the body-cavity, the muscle-plates themselves are oblong structures, with two walls enclosing the cavity just mentioned, in which the original ventral dilatation is still visible. The outer or somatic wall of the plates retains its previous simple constitution. The splanchnic wall has however a somewhat complicated structure. It is composed dorsally and ventrally of a columnar epithelium, but in its middle portion of the muscle-cells previously spoken of. Between these and the central cavity of the plates the epithelium forming the remainder of the layer commences to insert itself; so that between the first-formed muscle and the cavity of the muscle-plate there appears a thin layer of cells, not however continuous throughout.

At the end of the period *K* the muscle-plates have extended dorsally two-thirds of the way up the sides of the spinal cord, and ventrally to the level of the segmental duct. Their edges are not straight, but are bent into an angular form, with the apex pointing forwards. Vide Pl. vi. fig. 17 *mp*.

Before the end of the period a number of connective-tissue cells make their appearance, and extend upwards from the dorsal summit of the muscle-plates around the top of the spinal cord. These cells are at first rounded, but become

typical branched connective-tissue cells before the close of the period (Pl. v. fig. 7 and 8).

Between stages I and K the bodies of the vertebræ rapidly increase in size and send prolongations downwards and inwards to meet below the notochord.

These soon become indistinguishably fused with other cells which appear in the area between the alimentary cavity and the notochord, but probably serve alone to form the vertebral bodies, while the cells adjoining them form the basis for the connective tissue of the kidneys, &c.

The vertebral bodies also send prolongations dorsalwards between the sides of the spinal cord and the muscle-plates. These grow round till they meet above the spinal and enclose the dorsal nerve-roots. They soon however become fused with the dorsal prolongations from the muscle-plates, at least so far as my methods of investigation enable me to determine; but it appears to me probable that they in reality remain distinct, and become converted into the neural arches, while the connective-tissue cells from the muscle-plates form the adjoining subcutaneous and inter-muscular connective tissue.

All the cells of vertebral rudiments become stellate and form typical embryonic connective tissue. The rudiments however still retain their primitive segmentation, corresponding with that of the muscle-plates, and do not during this period acquire their secondary segmentation. Their segmentation is however less clear than it was at an earlier period, and in the dorsal part of the vertebral rudiments is mainly indicated by the dorsal nerve-roots, which always pass out in the interval between two vertebral rudiments. Vide Pl. VI. fig. 12 *pr*.

Intermediate Cell-Mass. At about the period when the muscle-plates become completely free, a fusion takes place between the somatopleure and splanchnopleure immediately above the dorsal extremity of the true body-cavity (Pl. v. fig. 6). The cells in the immediate neighbourhood of this fusion form a special mass, which we may call the intermediate cell-mass—a name originally used by Waldeyer for the homologous cells in the Chick. Out of it are developed the urino-genital organs and the adjoining tissues. At first it forms little more than a columnar epithelium, but by the close of the period is divided

into (1) An epithelium on the free surface; from this are derived the glandular parts of the kidneys and functional parts of the genital glands; and (2) a subjacent stroma which forms the basis for the connective tissue and vascular parts of these organs.

To the history of these parts a special section is devoted; and I now pass to the description of the mesoblast which lines the body-cavity and forms the connective tissue of the body-wall, and the muscular and connective tissue of the wall of the alimentary canal.

Body-Cavity and parietal plates. By the close of stage H, as has been already mentioned, a cavity is formed between the somatopleure and splanchnopleure in the anterior part of the trunk, which rapidly widens during the succeeding stages. Anteriorly, it invests the heart, which arises during stage G, as a simple space between the ventral wall of the throat and the splanchnopleure (Pl. v. fig. 4). Posteriorly it ends blindly.

This cavity forms in the region of the heart the rudiment of the pericardial cavity. The remainder of the cavity forms the true body-cavity.

Immediately behind the heart the alimentary canal is still open to the yolk-sac, and here naturally the two lateral halves of the body-cavity are separated from each other. In the tail of the embryo no body-cavity has appeared by stage I, although the parietal plates of mesoblast are distinctly divided into somatic and splanchnic layers. In the caudal region the lateral plates of mesoblast of the two sides do not unite ventrally, but are, on the contrary, quite disconnected. Their ventral edge is moreover much swollen (Pl. v. fig. 1). At the caudal swelling the mesoblast plates cease to be distinctly divided into somatopleure and splanchnopleure, and more or less fuse with the hypoblast of the caudal vesicle (Pl. v. fig. 2).

Between stages I and K the body-cavity extends backwards behind the point where the anus is about to appear, though it never reaches quite to the extreme end of the tail. The backward extension of the body-cavity, as is primitively the case everywhere, is formed of two independent lateral halves (Pl. VI. fig. 9 *a*). Anteriorly, opposite the hind end of the small intestine, these two lateral halves unite ventrally to

form a single cavity in which hangs the small intestine (Pl. v. fig. 8) suspended by a very short mesentery.

The most important change which takes place in the body-cavity during this period is the formation of a septum which separates off a pericardial cavity from the true body-cavity.

Immediately in front of the liver the splanchnic and somatic walls of the body come into very close contact, and I believe unite over the greater part of their extent. The septum so formed divides the original body-cavity into an anterior section or pericardial cavity, and a posterior section or true body-cavity. There is left, however, on each side dorsally a rather narrow passage which serves to unite the pericardial cavity in front with the true body-cavity behind.

In Pl. v. fig. 8 *a*, there is seen on one side a section through this passage, while on the other side the passage is seen to be connected with the pericardial cavity.

It is not possible from transverse sections to determine for certain whether the septum spoken of is complete. An examination of longitudinal horizontal sections from an embryo belonging to the close of the stage K has however satisfied me that this septum, by that stage at any rate, is fully formed.

The two lateral passages spoken of above probably unite in the adult to form the passage connecting the pericardial with the peritoneal cavity, which, though provided with but a single orifice into the pericardial cavity, divides into two limbs before opening into the peritoneal cavity.

The body-cavity undergoes no further changes of importance till the close of the period.

Somatopleure and Splanchnopleure. Both the somatic and splanchnic walls of the body-cavity during stage I exhibit a simple uniform character throughout their whole extent. They are formed of columnar cells where they line the dorsal part of the body-cavity, but ventrally of more rounded and irregular cells (Pl. v. fig. 5).

In them may occasionally be seen aggregations of very peculiar and large cells with numerous highly refracting spherules; the cells forming these are not unlike the *primitive ova* to be described subsequently, but are probably large cells derived from the yolk.

It is during the stage intermediate between I and K that the first changes become visible which indicate a distinction between an epithelium (endothelium) lining the body-cavity and the connective tissue adjoining this.

There are at first but very few connective-tissue cells between the epithelium of the somatic layer of the mesoblast and the epiblast, but a connection between them is established by peculiar protoplasmic processes which pass from the one to the other (Pl. V. fig. 8). Towards the end of stage K, however, there appears between the two a network of mesoblastic cells connecting them together. In the rudimentary outgrowth to form the limbs the mesoblast cells of the somatic layer are crowded in an especially dense manner.

From the first the connective-tissue cells around the hypoblastic epithelium of the alimentary tract are fairly numerous (Pl. V. fig. 8), and by the close of this period become concentrically arranged round the intestinal epithelium, though not divided into distinct layers. A special aggregation of them is present in the hollow of the rudimentary spiral valve.

Behind the anal region the two layers of the mesoblast (somatic and splanchnic) completely fuse during stage K, and form a mass of stellate cells in which no distinction into two layers can be detected (Pl. VI. fig. 9 *c*, 9 *d*).

The alimentary canal, which at first lies close below the aorta, becomes during this period gradually carried further and further from this, remaining however attached to the roof of the body-cavity by a thin layer of the mesoblast of the splanchnopleure formed of an epithelium on each side, and a few interposed connective-tissue cells. This is the mesentery which by the close of stage K is of considerable length in the region of the stomach, though shorter elsewhere.

The above account of the protovertebræ and body-cavity applies solely to the genera Pristiurus and Scyllium. The changes of these parts in Torpedo only differ from those of Pristiurus in unimportant though fairly noticeable details. Without entering into any full description of these it may be pointed out that both the true body-cavity and its continuations into

the protovertebræ appear later in Torpedo than in Pristiurus and Scyllium. In some cases even the muscle-plates become definitely separated and independent before the true body-cavity has appeared. As a result of this the primitive continuity of the body-cavity and cavity of the muscle-plates becomes to a certain extent masked, though its presence may easily be detected by the obvious continuity which at first exists between the somatic and splanchnic layers of mesoblast and the two layers of the muscle-plate. In the muscle-plate itself the chief point to be noticed is the fact that the earlier formed bands of muscles (mp') arise very much later, and are less conspicuous, in Torpedo than in the genera first described. They are however present and functional.

The anatomical relations of the body-cavity itself are precisely the same in Torpedo as in Pristiurus and Scyllium, and the pericardial cavity becomes separated from the peritoneal in same way in all the genera; the two lateral canals connecting the two cavities being also present in all the three genera. The two independent parietal plates of mesoblast of the posterior parts of the body have ventrally a swollen edge, as in Pristiurus, and in this a cavity appears which forms a posterior continuation of the true body-cavity.

Resumé. The primitive independent mesoblast plates of the two sides of the body become divided into two layers, a somatic and a splanchnic (Hautfaserblatt and Darmfaserblatt). At the same time in the dorsal part of the mesoblast plate a series of transverse splits appear and serve to distinguish a dorsal or vertebral part of the plate from a ventral or parietal part.

Between the somatic and splanchnic layers of the mesoblast plate a cavity arises which is continued quite to the summit of the vertebral part of the plate. This is the primitive body-cavity; and at first the cavity is divided into two lateral and independent halves.

The next change which takes place is the complete separation of the vertebral portion of the plate from the parietal; thereby the upper segmented part of the body-cavity becomes isolated and separated from the lower and unsegmented part. In connection with this change in the constitution of the body-cavity there are formed a series of rectangular plates, each com-

posed of two layers, a somatic and a splanchnic, between which is the cavity originally continuous with the body-cavity. The splanchnic layer of the plates buds off cells to form the rudiments of the vertebral bodies which are originally segmented in the same planes as the protovertebræ. The plates themselves remain as the muscle-plates and develop a special layer of muscle (*m p′*) in their splanchnic layer.

In the meantime the parietal plates of the two sides unite ventrally throughout the intestinal and cardiac regions of the body, and the two primitively isolated cavities contained in them coalesce. Posteriorly however the plates do not unite ventrally, and their contained cavities remain distinct.

At first the pericardial cavity is quite continuous with the body-cavity; but by the close of the period included in the present chapter it becomes separated from the body-cavity by a septum in front of the liver, which is however pierced dorsally by two narrow channels.

The parts derived from the two layers of the mesoblast (not including special organs or the vascular system) are as follow:—

From the somatic layer are formed

(1) A considerable part of the voluntary muscular system of the body.
(2) The dermis.
(3) A large part of the intermuscular connective tissue.
(4) Part of the peritoneal epithelium.

From the splanchnic layer are formed

(1) A great part of the voluntary muscular system.
(2) Part of the intermuscular connective tissue (?).
(3) The axial skeleton.
(4) The muscular and connective-tissue wall of the alimentary tract.
(5) A great part of the peritoneal epithelium.

General Considerations. In the history which has just been given of the development of the mesoblast, there are several points which appear to me to throw light upon the primitive origin of that layer. Before entering into these it is however necessary to institute a comparison between the history of the

mesoblast in Elasmobranchs and in other Vertebrates, in order to distinguish as far as possible the primitive and the secondary characters present in the various groups.

Though the Mammals are to be looked on as the most differentiated group amongst the Vertebrates, yet in their embryonic history they retain many very primitive features, and, as has been recently shewn by Hensen[1], present numerous remarkable approximations to the Elasmobranchs. We find accordingly[2] that the primitive lateral plates of mesoblast undergo nearly the same changes in these two groups. In Mammals there is at first a continuous cavity extending through both the parietal and vertebral portions of each plate, and dividing the plates into a somatic and a splanchnic layer: this cavity is the primitive body-cavity. The vertebral portion of each plate with its contained cavity then becomes divided off from the parietal. The later development of these parts is not accurately known, but it seems that the outer portion of each vertebral plate, composed of two layers (somatic and splanchnic) enclosing between them a remnant of the primitive body-cavity, becomes separated off as a muscle-plate. The remainder forms a vertebral rudiment, &c. Thus the extension of the body-cavity into the vertebral portion of the mesoblast, and the constriction of the vertebral portion of the cavity from the remainder, are as distinctive features of Mammals as they are of the Elasmobranchs.

In Birds[3] horizontal splitting of the mesoblast into somatic and splanchnic layers appears, as in Mammals, to extend at first to the summit of the protovertebræ, but these bodies become so early separated from the parietal plates that this fact has usually been overlooked or denied; but even on the second day of incubation the outer layer of the protovertebræ is continuous with the somatic layer of the lateral plates, and the inner layer and kernel of the protovertebræ with the splanchnic layer of the lateral plates[4]. After the isolation

[1] *Zeitschrift f. Anat. Entwicklungsgeschichte*, Vol. I.

[2] Hensen *loc. cit.*

[3] For the history of protovertebræ and muscle-plates in Birds, vide *Elements of Embryology*, Foster and Balfour. The statement there made that the horizontal splitting of the mesoblast does not extend to the summit of the vertebral plate, must however be regarded as doubtful.

[4] Vide *Elements of Embryology*, p. 56.

muscle-band just described, begins to proliferate, and produce a number of cells, which at once grow in between the muscles and the notochord. These cells are very easily seen both in transverse and longitudinal sections, and form the commencing vertebral bodies (Pl. v. fig. 6, and Pl. vi. fig. 10 and 11 *Vr*).

At first the vertebral bodies have the same segmentation as the protovertebræ from which they sprang; that is to say, they form masses of embryonic cells separated from each other by narrow slits, continuous with the slits separating the protovertebræ. They have therefore at their first appearance a segmentation completely different from that which they eventually acquire (Pl. vi. fig. 11).

After the separation of the vertebral bodies from the protovertebræ, the remaining parts of the protovertebræ may be called muscle-plates; since they become directly converted into the whole voluntary muscular system of the trunk. At the time when the cavity of the muscle-plates has become completely separate from the body-cavity, the muscle-plates themselves are oblong structures, with two walls enclosing the cavity just mentioned, in which the original ventral dilatation is still visible. The outer or somatic wall of the plates retains its previous simple constitution. The splanchnic wall has however a somewhat complicated structure. It is composed dorsally and ventrally of a columnar epithelium, but in its middle portion of the muscle-cells previously spoken of. Between these and the central cavity of the plates the epithelium forming the remainder of the layer commences to insert itself; so that between the first-formed muscle and the cavity of the muscle-plate there appears a thin layer of cells, not however continuous throughout.

At the end of the period *K* the muscle-plates have extended dorsally two-thirds of the way up the sides of the spinal cord, and ventrally to the level of the segmental duct. Their edges are not straight, but are bent into an angular form, with the apex pointing forwards. Vide Pl. vi. fig. 17 *mp*.

Before the end of the period a number of connective-tissue cells make their appearance, and extend upwards from the dorsal summit of the muscle-plates around the top of the spinal cord. These cells are at first rounded, but become

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These soon become indistinguishably fused with other cells which appear in the area between the alimentary cavity and the notochord, but probably serve alone to form the vertebral bodies, while the cells adjoining them form the basis for the connective tissue of the kidneys, &c.

The vertebral bodies also send prolongations dorsalwards between the sides of the spinal cord and the muscle-plates. These grow round till they meet above the spinal and enclose the dorsal nerve-roots. They soon however become fused with the dorsal prolongations from the muscle-plates, at least so far as my methods of investigation enable me to determine; but it appears to me probable that they in reality remain distinct, and become converted into the neural arches, while the connective-tissue cells from the muscle-plates form the adjoining subcutaneous and inter-muscular connective tissue.

All the cells of vertebral rudiments become stellate and form typical embryonic connective tissue. The rudiments however still retain their primitive segmentation, corresponding with that of the muscle-plates, and do not during this period acquire their secondary segmentation. Their segmentation is however less clear than it was at an earlier period, and in the dorsal part of the vertebral rudiments is mainly indicated by the dorsal nerve-roots, which always pass out in the interval between two vertebral rudiments. Vide Pl. VI. fig. 12 *pr.*

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This cavity forms in the region of the heart the rudiment of the pericardial cavity. The remainder of the cavity forms the true body-cavity.

Immediately behind the heart the alimentary canal is still open to the yolk-sac, and here naturally the two lateral halves of the body-cavity are separated from each other. In the tail of the embryo no body-cavity has appeared by stage I, although the parietal plates of mesoblast are distinctly divided into somatic and splanchnic layers. In the caudal region the lateral plates of mesoblast of the two sides do not unite ventrally, but are, on the contrary, quite disconnected. Their ventral edge is moreover much swollen (Pl. V. fig. 1). At the caudal swelling the mesoblast plates cease to be distinctly divided into somatopleure and splanchnopleure, and more or less fuse with the hypoblast of the caudal vesicle (Pl. V. fig. 2).

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form a single cavity in which hangs the small intestine (Pl. V. fig. 8) suspended by a very short mesentery.

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Immediately in front of the liver the splanchnic and somatic walls of the body come into very close contact, and I believe unite over the greater part of their extent. The septum so formed divides the original body-cavity into an anterior section or pericardial cavity, and a posterior section or true body-cavity. There is left, however, on each side dorsally a rather narrow passage which serves to unite the pericardial cavity in front with the true body-cavity behind.

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It is not possible from transverse sections to determine for certain whether the septum spoken of is complete. An examination of longitudinal horizontal sections from an embryo belonging to the close of the stage K has however satisfied me that this septum, by that stage at any rate, is fully formed.

The two lateral passages spoken of above probably unite in the adult to form the passage connecting the pericardial with the peritoneal cavity, which, though provided with but a single orifice into the pericardial cavity, divides into two limbs before opening into the peritoneal cavity.

The body-cavity undergoes no further changes of importance till the close of the period.

Somatopleure and Splanchnopleure. Both the somatic and splanchnic walls of the body-cavity during stage I exhibit a simple uniform character throughout their whole extent. They are formed of columnar cells where they line the dorsal part of the body-cavity, but ventrally of more rounded and irregular cells (Pl. V. fig. 5).

In them may occasionally be seen aggregations of very peculiar and large cells with numerous highly refracting spherules; the cells forming these are not unlike the *primitive ova* to be described subsequently, but are probably large cells derived from the yolk.

It is during the stage intermediate between I and K that the first changes become visible which indicate a distinction between an epithelium (endothelium) lining the body-cavity and the connective tissue adjoining this.

There are at first but very few connective-tissue cells between the epithelium of the somatic layer of the mesoblast and the epiblast, but a connection between them is established by peculiar protoplasmic processes which pass from the one to the other (Pl. v. fig. 8). Towards the end of stage K, however, there appears between the two a network of mesoblastic cells connecting them together. In the rudimentary outgrowth to form the limbs the mesoblast cells of the somatic layer are crowded in an especially dense manner.

From the first the connective-tissue cells around the hypoblastic epithelium of the alimentary tract are fairly numerous (Pl. v. fig. 8), and by the close of this period become concentrically arranged round the intestinal epithelium, though not divided into distinct layers. A special aggregation of them is present in the hollow of the rudimentary spiral valve.

Behind the anal region the two layers of the mesoblast (somatic and splanchnic) completely fuse during stage K, and form a mass of stellate cells in which no distinction into two layers can be detected (Pl. vi. fig. 9 *c*, 9 *d*).

The alimentary canal, which at first lies close below the aorta, becomes during this period gradually carried further and further from this, remaining however attached to the roof of the body-cavity by a thin layer of the mesoblast of the splanchnopleure formed of an epithelium on each side, and a few interposed connective-tissue cells. This is the mesentery which by the close of stage K is of considerable length in the region of the stomach, though shorter elsewhere.

The above account of the protovertebræ and body-cavity applies solely to the genera Pristiurus and Scyllium. The changes of these parts in Torpedo only differ from those of Pristiurus in unimportant though fairly noticeable details. Without entering into any full description of these it may be pointed out that both the true body-cavity and its continuations into

the protovertebræ appear later in Torpedo than in Pristiurus and Scyllium. In some cases even the muscle-plates become definitely separated and independent before the true body-cavity has appeared. As a result of this the primitive continuity of the body-cavity and cavity of the muscle-plates becomes to a certain extent masked, though its presence may easily be detected by the obvious continuity which at first exists between the somatic and splanchnic layers of mesoblast and the two layers of the muscle-plate. In the muscle-plate itself the chief point to be noticed is the fact that the earlier formed bands of muscles (*mp'*) arise very much later, and are less conspicuous, in Torpedo than in the genera first described. They are however present and functional.

The anatomical relations of the body-cavity itself are precisely the same in Torpedo as in Pristiurus and Scyllium, and the pericardial cavity becomes separated from the peritoneal in same way in all the genera; the two lateral canals connecting the two cavities being also present in all the three genera. The two independent parietal plates of mesoblast of the posterior parts of the body have ventrally a swollen edge, as in Pristiurus, and in this a cavity appears which forms a posterior continuation of the true body-cavity.

Resumé. The primitive independent mesoblast plates of the two sides of the body become divided into two layers, a somatic and a splanchnic (Hautfaserblatt and Darmfaserblatt). At the same time in the dorsal part of the mesoblast plate a series of transverse splits appear and serve to distinguish a dorsal or vertebral part of the plate from a ventral or parietal part.

Between the somatic and splanchnic layers of the mesoblast plate a cavity arises which is continued quite to the summit of the vertebral part of the plate. This is the primitive body-cavity; and at first the cavity is divided into two lateral and independent halves.

The next change which takes place is the complete separation of the vertebral portion of the plate from the parietal; thereby the upper segmented part of the body-cavity becomes isolated and separated from the lower and unsegmented part. In connection with this change in the constitution of the body-cavity there are formed a series of rectangular plates, each com-

posed of two layers, a somatic and a splanchnic, between which is the cavity originally continuous with the body-cavity. The splanchnic layer of the plates buds off cells to form the rudiments of the vertebral bodies which are originally segmented in the same planes as the protovertebræ. The plates themselves remain as the muscle-plates and develop a special layer of muscle (*m p'*) in their splanchnic layer.

In the meantime the parietal plates of the two sides unite ventrally throughout the intestinal and cardiac regions of the body, and the two primitively isolated cavities contained in them coalesce. Posteriorly however the plates do not unite ventrally, and their contained cavities remain distinct.

At first the pericardial cavity is quite continuous with the body-cavity; but by the close of the period included in the present chapter it becomes separated from the body-cavity by a septum in front of the liver, which is however pierced dorsally by two narrow channels.

The parts derived from the two layers of the mesoblast (not including special organs or the vascular system) are as follow:—

From the somatic layer are formed

(1) A considerable part of the voluntary muscular system of the body.
(2) The dermis.
(3) A large part of the intermuscular connective tissue.
(4) Part of the peritoneal epithelium.

From the splanchnic layer are formed

(1) A great part of the voluntary muscular system.
(2) Part of the intermuscular connective tissue (?).
(3) The axial skeleton.
(4) The muscular and connective-tissue wall of the alimentary tract.
(5) A great part of the peritoneal epithelium.

General Considerations. In the history which has just been given of the development of the mesoblast, there are several points which appear to me to throw light upon the primitive origin of that layer. Before entering into these it is however necessary to institute a comparison between the history of the

mesoblast in Elasmobranchs and in other Vertebrates, in order to distinguish as far as possible the primitive and the secondary characters present in the various groups.

Though the Mammals are to be looked on as the most differentiated group amongst the Vertebrates, yet in their embryonic history they retain many very primitive features, and, as has been recently shewn by Hensen[1], present numerous remarkable approximations to the Elasmobranchs. We find accordingly[2] that the primitive lateral plates of mesoblast undergo nearly the same changes in these two groups. In Mammals there is at first a continuous cavity extending through both the parietal and vertebral portions of each plate, and dividing the plates into a somatic and a splanchnic layer: this cavity is the primitive body-cavity. The vertebral portion of each plate with its contained cavity then becomes divided off from the parietal. The later development of these parts is not accurately known, but it seems that the outer portion of each vertebral plate, composed of two layers (somatic and splanchnic) enclosing between them a remnant of the primitive body-cavity, becomes separated off as a muscle-plate. The remainder forms a vertebral rudiment, &c. Thus the extension of the body-cavity into the vertebral portion of the mesoblast, and the constriction of the vertebral portion of the cavity from the remainder, are as distinctive features of Mammals as they are of the Elasmobranchs.

In Birds[3] horizontal splitting of the mesoblast into somatic and splanchnic layers appears, as in Mammals, to extend at first to the summit of the protovertebræ, but these bodies become so early separated from the parietal plates that this fact has usually been overlooked or denied; but even on the second day of incubation the outer layer of the protovertebræ is continuous with the somatic layer of the lateral plates, and the inner layer and kernel of the protovertebræ with the splanchnic layer of the lateral plates[4]. After the isolation

[1] *Zeitschrift f. Anat. Entwicklungsgeschichte*, Vol. I.

[2] Hensen *loc. cit.*

[3] For the history of protovertebræ and muscle-plates in Birds, vide *Elements of Embryology*, Foster and Balfour. The statement there made that the horizontal splitting of the mesoblast does not extend to the summit of the vertebral plate, must however be regarded as doubtful.

[4] Vide *Elements of Embryology*, p. 56.

of the protovertebræ the primitive position of the split which separated their somatic and splanchnic layers becomes obscured, but when on the third day the muscle-plates are formed they are found to be *constituted of two layers, an inner and an outer, which enclose between them a central cavity.* This remarkable fact, which has not received much attention, though noticeable in most figures, receives a simple explanation on Darwinian principles. The central cavity of the muscle-plate is, in fact, a remnant of vertebral extension of the body-cavity, and is the same cavity as that found in the muscle-plates of Elasmobranchs. The two layers of the muscle-plate also correspond with the two layers present in Elasmobranchs, the one belonging to the somatic, the other to the splanchnic layer of mesoblast. The remainder of the protovertebræ internal to the muscle-plates is very large in Birds, and is the equivalent of that portion of the protovertebræ which in Elasmobranchs is split off to form the vertebral bodies[1] (Pl. v. fig. 6, 7, 8, *Vr*). Thus, though the history of the development of the mesoblast is not precisely the same for Birds as for Elasmobranchs, yet the differences between the two groups are of such a character as to prove in a striking manner that the Avian development is a derivation from a more primary form, like that of the Elasmobranchs.

According to the statements of Bambeke and Götte, the Amphibians present rather remarkable peculiarities in the development of their muscular system. Each side-plate of mesoblast is divided into a somatic and a splanchnic layer, continuous throughout the vertebral and parietal portions of the plate. The vertebral portions (protovertebræ) of the plates soon become separated from the parietal, and form an independent mass of cells constituted of two layers, which were originally continuous with the somatic and splanchnic layers of the parietal plates. The outer or somatic layer of the

[1] Dr Götte, *Entwicklungsgeschichte der Unke*, p. 534, gives a different account of the development of the protovertebræ from that in the text. He states that the muscle-plates do not give rise to the main dorso-lateral muscles, but only to some superficial ventral muscles, while the dorso-lateral muscles are according to him formed from part of the kernel of the protovertebræ internal to the muscle-plates. The account given in the text is the result of my own investigations, and accords precisely with the recent statements of Professor Kölliker, *Entwicklungsgeschichte*, 1876.

vertebral plates is formed of a single row of cells, but the inner or splanchnic layer is made up of a central kernel of cells and an inner single layer. This central kernel is the first portion of the vertebral body to undergo any change, and it becomes converted into the main dorso-lateral muscles of the body, which apparently correspond with the muscles derived from the whole muscle-plate of the Elasmobranchs. From the inner layer of the splanchnic division there are next formed the main internal ventral muscles, rectus abdominis, &c., as well as the chief connective-tissue elements of the parts surrounding the spinal cord. The outer layer of the vertebral plates forms the dermis and sub-cutaneous connective tissue, as well as some of the superficial muscles of the trunk and the muscles of the limbs.

Dr Götte appears to think that the vertebral plates in Amphibians present a perfectly normal development very similar to that of other Vertebrates. The divergences between Amphibians and other Vertebrates appear, however, to myself, to be very great, and although the very careful account given by Dr Götte is probably to be relied on, yet some further explanation than he has offered of the development of these parts amongst the Amphibians would seem to be required.

A primary stage in which the two layers of the vertebral plates are continuous with the somatic and splanchnic layers of a body-wall is equally characteristic of Amphibians, Elasmobranchs and Mammals. In the subsequent development, however, a great difference between the types becomes apparent, for whereas in Elasmobranchs both layers of the vertebral plates combine to form the muscle-plates, out of which the great dorso-lateral muscles are formed, in Amphibians what appear to be the equivalent muscles are derived from a few of the cells (the kernel) of the inner layer of the vertebral plates only. The cells which form the lateral muscles in Amphibians might be thought to correspond in position with the cells which become, in Elasmobranchs, converted into the special early formed band of muscles (*m. p'.*), rather than, as their development seems to indicate, with the whole Elasmobranch muscle-plates[1].

[1] A view by which the early formed muscles in Elasmobranch could be regarded as homologous with the muscle-kernel of the Amphibian embryo is very tempt-

Osseous Fishes are stated to agree with Amphibians in the development of their protovertebræ and muscular system[1], but further observations on this point are required.

Though the development of the general muscular system and muscle-plates does not, according to existing statements, take place on quite the same type throughout the Vertebrate sub-kingdom, yet the comparison which has been instituted between Elasmobranchs and other Vertebrates appears to prove that there are one or two common features in their development, which may be regarded as primitive, and as having been inherited from the ancestors of Vertebrates. These features are (1) The extension of the body-cavity into the vertebral plates, and subsequent enclosure of this cavity between the two layers of the muscle-plates; (2) The primitive division of the vertebral plate into a somatic and a splanchnic layer, and the formation of a large part of the voluntary muscular system out of the splanchnic layer.

The ultimate derivation of the mesoblast forms one of the numerous burning questions of modern embryology, and there are advocates to be found for almost every one of the possible views the question admits of.

All who accept the doctrine of descent are agreed that primitively only two embryonic layers were present — the epiblast and the hypoblast—and that the mesoblast subsequently appeared as a distinct layer, after a certain complexity of organization had been attained.

The general agreement stops, however, at this point, and the greatest divergence of opinion exists with reference to all further questions which bear on the development of the mesoblast. There appear to be four possibilities as to the origin of this layer.

It may be derived:

(1) entirely from the epiblast,

ing and in some ways plausible, but Dr Götte's account would require very considerable modification before such a view could be seriously entertained. Since, however, the development of the muscular system in Elasmobranchs has not been dealt with in detail, a discussion of its homologies must be deferred.

[1] Ehrlich, Ueber den peripher. Theil d. Urwirbel. *Archiv f. Mic. Anat.* Vol. II.

(2) partly from the epiblast, and partly from the hypoblast,
(3) entirely from the hypoblast,
(4) or may have no fixed origin.

The fourth of these possibilities may for the present be dismissed, since it can be only maintained should it turn out that all the other views are erroneous. The first possibility is supported by the case of the Cœlenterata, and we might almost say by that of this group only[1].

Amongst the Cœlenterata the mesoblast, when present, is unquestionably a derivative of the epiblast, and when, as is frequently the case, a distinct mesoblast is not present, the muscle-cells form a specialized part of the epidermic cells.

The condition of the mesoblast in these lowly organized animals is exactly what might *a priori* have been anticipated, but the absence throughout the group of a true body-cavity, or specially developed muscular system of the alimentary tract, prevents the possibility of generalizing for other groups, from the condition of the mesoblast in this one.

In those animals in which a body-cavity and muscular alimentary tract are present, it would certainly appear reasonable to expect the mesoblast to be derived from both the primitive layers: the voluntary muscular system from epiblast, and the splanchnic system from the hypoblast. This view has been taken and strongly advocated by so distinguished an embryologist as Professor Haeckel, and it must be admitted, that on *à priori* grounds there is much to recommend it; there are, however, so far as I am aware of, comparatively few observed facts in its favour.

Professor Haeckel's own objective arguments in support of his view are as follows:

(1) From the fact that some investigators derive the meso-

[1] The most important other instances in addition to that of the Cœlenterata which can be adduced in favour of the epiblastic origin of the mesoblast are the Bird and Mammal, in which according to the recent observations of Hensen for the Mammal, and Kölliker for the Mammal and Bird, the mesoblast is split off from the epiblast. If the views I have elsewhere put forward about the meaning of the primitive groove be accepted, the derivation of the mesoblast from the epiblast in these instances would be apparent rather than real, and have no deep morphological significance for the present question.

Other instances may be brought forward from various groups, but none of these are sufficiently well confirmed to be of any value in the determination of the present question.

blast with absolute confidence from the hypoblast, while others do so with equal confidence from the epiblast, he concludes that it is really derived from both these layers.

(2) A second argument is founded on the supposed derivation of the mesoblast in Amphioxus from both epiblast and hypoblast. Kowalevsky's account (on which apparently Prof. Haeckel's[1] statements are based) appears to me, however, too vague, and his observations too imperfect, for much confidence to be placed in his statements on this head. It does not indeed appear to me that the formation of the layers in Amphioxus, till better known, can be used as an argument for any special view about this question.

(3) Professor Haeckel's own observations on the development of Osseous fish form a third argument in support of his views. These observations do not, however, accord with those of the majority of investigators, and not having been made by means of sections, require further confirmation before they can be definitely accepted.

(4) A fourth argument rests on the fact that the various embryonic layers fuse together to form the primitive streak or axis-cord in higher vertebrates. This he thinks proves that the mesoblast is derived from both the primitive layers. The primitive streak has, however, according to my views, quite another significance to that attributed to it by Professor Haeckel[2]; but in any case Professor Kölliker's researches, and on this point my own observations accord with his, appear to me to prove that the fusion which there takes place is only capable of being used as an argument in favour of an epiblastic origin of the mesoblast, and not of its derivation from both epiblast and hypoblast.

The objective arguments in favour of Professor Haeckel's views are not very conclusive, and he himself does not deny that the mesoblast as a rule apparently arises as a single and undivided mass from one of the two primary layers, and only subsequently becomes split into somatic and splanchnic strata. This original fusion and subsequent splitting of the mesoblast

[1] Vide *Anthropogenie*, p. 197.

[2] Vide Self, Development of Elasmobranch Fishes, *Journal of Anat. and Phys.* Vol. x. note on p. 682, and also Review of Professor Kölliker's Entwicklungsgeschichte des Menschen u. d. höheren Thiere, *Journal of Anat. and Phys.* Vol. x.

is explained by him as a secondary condition, a possibility which cannot by any means be thrown on one side. It seems therefore worth while examining how far the history of the somatic and splanchnic layers of the mesoblast in Elasmobranchs and other Vertebrates accords with the supposition that they were primitively split off from the epiblast and the hypoblast respectively.

It is well to consider first of all what parts of the mesoblast of the body might be expected to be derived from the somatic and splanchnic layers on this view of their origin[1].

From the somatic layer of the mesoblast there would no doubt be formed the whole of the voluntary muscular system of the body, the dermis, the subcutaneous connective tissue, and the connective tissue between the muscles. It is probable also, though this point is less certain, that the skeleton would be derived from the somatic layer. From the splanchnic layer would be formed the connective tissue and muscular layers of the alimentary tract, and possibly also the vascular system.

Turning to the actual development of these parts, the discrepancy between theory and fact becomes very remarkable. From the somatic layer of the mesoblast, part of the voluntary muscular system and the dermis is no doubt derived, but the splanchnic layer supplies the material, not only for the muscular wall of the digestive canal and the vascular system, but also for the whole of the axial skeleton *and a great part of the voluntary muscular system of the body, including the first-formed muscles.* Though remarkable, it is nevertheless not inconceivable, that the skeleton might be derived from the splanchnic mesoblast, but it is very difficult to understand how there could be formed from it a part of the voluntary muscular system of the body indistinguishably fused with part of the muscular system derived from the somatopleure.

[1] Professor Haeckel speaks of the splitting of the mesoblast in Vertebrates into a somatic and splanchnic layer as a secondary process (*Gastrula u. Eifurchung d. Thiere*), but does not make it clear whether he regards this secondary splitting as taking place along the old lines. It appears to me to be fairly certain that even if the original unsplit condition of the mesoblast is to be regarded as a secondary condition, yet that the splitting of this must take place along the old lines, otherwise a change in the position of the body-cavity in the adult would have to be supposed—an unlikely change producing unnecessary complication. The succeeding argument is based on the assumption that the unsplit condition is a secondary condition, but that the split which eventually appears in this occurs along the old lines, separating the primitive splanchnopleure from the primitive somatopleure.

No fact in my investigations comes out more clearly than that a great part of the voluntary muscular system is formed from the splanchnic layer of the mesoblast, yet this fact presents a most serious difficulty to the view that the somatic and splanchnic layers of the mesoblast in Vertebrates are respectively derived from the epiblast and hypoblast.

In spite, therefore, of general *à priori* considerations of a very convincing kind which tell in favour of the double origin of the mesoblast, this view is supported by so few objective facts, and there exists so powerful an array of facts against it, that at present, at least, it seems impossible to maintain it. The full strength of the facts against it will appear more fully in a review of the present state of our knowledge as to the development of the mesoblast in the different groups. To this I now pass.

In a paper on the "Early stages of development in Vertebrates[1]" a short resumé was given of the development of the mesoblast throughout the animal kingdom, which it may be worth while repeating here with a few additions. So far as we know at present, the mesoblast is derived from the hypoblast in the following groups:

Echinoderms (Hensen, Agassiz, Metschnikoff, Selenka, Götte), Nematodes (Butschli), Sagitta (Kowalevsky, Butschli), Lumbricus and probably other Annelids (Kowalevsky), Brachiopoda (Kowalevsky), Crustaceans (Bobretzky), Insects (Kowalevsky, Ulianin, Dohrn), Myriapods (Metschnikoff), Tunicates (Kowalevsky, Kuppfer), Petromyzon (Owsjanikoff), Osseous fishes (Oellacher, Götte, Kowalevsky), Elasmobranchs (Self), Amphibians (Remak, Stricker, Götte).

The list includes members from the greater number of the groups of the animal kingdom; the most striking omissions being the Cœlenterates, Mollusks, and the Amniotic Vertebrates. The absence of the Cœlenterates has been already explained, and my grounds for regarding the Amniotic Vertebrates as apparent rather than real exceptions have also been pointed out. The Mollusks, however, remain as a large group, in which we as yet know very little as to the formation of the mesoblast.

[1] *Quart. Jl. of Micros. Science*, July, 1875.

Dr Rabl[1], who seems recently to have studied the development of Lymnæus by means of sections, gives some figures shewing the origin of the mesoblast; they are, however, too diagrammatic to be of much service in settling the present question, and the memoirs of Professor Lankester[2] and Dr Fol[3] are equally inconclusive for this purpose, for, though they contain figures of elongated and branched mesoblast cells passing from the epiblast to the hypoblast, no satisfactory representations are given of the origin of these cells. I have myself observed in embryos of Turbo or Trochus similar elongated cells to those figured by Lankester and Fol, but was unable clearly to determine whence they arose. The most accurate observations which we have on this question are those of Professor Bobretzky[4]. In Nassa he finds that the three embryonic layers are all established during segmentation. The outermost and smallest cells form the epiblast, somewhat larger cells adjoining these the mesoblast, and the large yolk-cells the hypoblast. These observations do not, however, demonstrate from which of the primary layers the mesoblast is derived.

The evidence at present existing is clearly in favour of the mesoblast being, in almost all groups of animals, developed from the hypoblast, but strong as this evidence is, it has not its full weight unless the actual manner in which the mesoblast is in many groups derived from the hypoblast, is taken into consideration. The most important of these are the Echinoderms, Brachiopods and Sagitta.

In the Echinoderms the mesoblast is in part formed by cells budded off from the hypoblast, *the remainder, however, arises as one or more diverticula of the alimentary tract.* From the separate cells first budded off there are formed the cutis, part of the connective tissue and the calcareous skeleton. The diverticula from the alimentary cavity form the water-vascular system and the somatic and splanchnic layers of mesoblast. *The cavity of the diverticula after the separation of the water-vascular system, forms the body-cavity. The outer lining layer of the cavity forms the somatic layer of mesoblast and the voluntary muscles; the*

[1] *Jenaische Zeitschrift*, Vol. IX.
[2] *Quart. Jl. of Micros. Science*, Vol. XXV. 1874, and *Phil. Trans.* 1875.
[3] *Archives de Zoologie*, Vol. IV.
[4] *Archiv f. Micr. Anat.* Vol. XIII.

inner lining layer the splanchnic mesoblast which unites with the epithelium of the alimentary tract. Though this fundamental arrangement would seem to be universal amongst Echinoderms, considerable variations of it are exhibited in different groups.

There is *one* outgrowth from the alimentary tract in Synapta; *two* in Echinoids, Asteroids and Ophiura; *three* in Comatula, and four (?) in Amphiura. The cavity of the outgrowth usually forms the body-cavity, but sometimes in Ophiura and Amphiura (Metschnikoff) the outgrowths are from the first or soon become solid, and only secondarily acquire a cavity, which is however homologous with the body-cavity of the other groups.

In Sagitta[1] the formation of the mesoblast and the alimentary tract takes place in nearly the same fashion as in the Echinoderms. The simple invaginate alimentary cavity becomes divided into three lobes, a central and two lateral. The two lateral lobes are gradually more and more constricted off from the central one, and become eventually quite separated from it; their cavities remain independent, *and form in the adult the body-cavity,* divided by a mesentery into two distinct lateral sections. *The inner layer of each of the two lateral lobes forms the mesoblast of the splanchnopleure, the outer layer the mesoblast of the somatopleure.* The central division of the primitive gastræa cavity remains as the alimentary tract of the adult.

The remarkable observations of Kowalevsky[2] on the development of the Brachiopoda have brought to light the unexpected fact that in two genera at least (Argiope and Terebratula) the mesoblast and body-cavity develope as paired constrictions from the alimentary tract in a manner almost identically the same as in Sagitta.

It thus appears that, so far as can be determined from the facts at our disposal, the mesoblast in almost all cases is derived from the hypoblast, and in three widely separated groups it arises as a pair of diverticula from the alimentary tract, each diverticulum containing a cavity which eventually becomes the

[1] Kowalevsky, Würmer u. Arthropoden, *Mém. Acad. Pétersbourg,* 1871.

[2] Zur Entwicklungsgeschichte d. Brachiopoden Protokoll d. Ersten Session der Versammlung Russischer Naturforscher i. Kasan, 1873. Published in *Kaiserliche Gesellschaft Moskau,* 1874 (Russian). Abstracted in Hoffmann and Schwalbe, *Jahresbericht f.* 1873.

body-cavity. I have elsewhere suggested[1] that the origin of the mesoblast from alimentary diverticula is to be regarded as primitive for all higher animals, and that the more general cases in which the mesoblast becomes split off, as an undivided layer, from the hypoblast, are in reality derivates from this. The chief obstacle in the way of this view arises from the difficulty of understanding how the whole voluntary muscular system can have been derived at first from the alimentary tract. That part of a voluntary system of muscles might be derived from the contractile diverticula of the alimentary canal attached to the body-wall is not difficult to understand, but it is not easy to believe that the secondary system so formed could completely replace the primitive muscular system, derived, as it must have been, from the epiblast. In my paper above quoted will be found various speculative suggestions for removing this difficulty, which I do not repeat here. If it be granted, however, that in Sagitta, Brachiopods, and Echinoderms we have genuine examples of the formation of the whole mesoblast from alimentary diverticula, it is easy to see how the formation of the mesoblast in Vertebrates may be a second derivate from an origin of this nature.

An attempt has been already made to shew that the mesoblast in Elasmobranchs is formed in a very primitive fashion, and for this reason the Elasmobranchs appear to be especially adapted for determining whether any signs are exhibited of a derivation of the mesoblast as paired diverticula of the alimentary tract. There are, it appears to me, several such features. In the first place, the mesoblast is split off from the hypoblast not as a single mass but as a pair of distinct masses, comparable with the paired diverticula already alluded to. Secondly, the body-cavity when it appears in the mesoblast plates, *does not arise as a single cavity, but as a pair of cavities, one for each plate of mesoblast,* and these cavities remain permanently distinct in some parts of the body, and nowhere unite till a comparatively late period. Thirdly, the primitive body-cavity of the embryo is not confined to the region in which a body-cavity exists in the adult, *but extends to the*

[1] Comparison of Early Stages, *Quart. Jl. Micros. Science*, July, 1875.

summit of the muscle-plates, at first separating parts which become completely fused in the adult to form the great lateral muscles of the body. It is difficult to understand how the body-cavity could have such an extension as this, on the supposition that it represents a primitive split in the mesoblast between the wall of the gut and the body-wall; but its extension to this part is quite intelligible, on the supposition that it represents the cavities of two diverticula of the alimentary tract, from whose muscular walls the voluntary muscular system has been derived. Lastly, I would point out that the derivation of part of the muscular system from what appears as the splanchnopleure is quite intelligible on the assumed hypothesis, but, as far as I see, on no other.

Such are the main features presented by the mesoblast in Elasmobranchs, which favour the view of its having originally formed the walls of the alimentary diverticula. Against this view of its nature are the facts (1) of the mesoblast plates being at first solid, and (2), as a consequence of this, of the body-cavity never communicating with the alimentary canal. These points, in view of our knowledge of embryological modifications, cannot be regarded as great difficulties to my view. We have many examples of organs, which, though in most cases arising as involutions, yet appear in other cases as solid ingrowths. Such examples are afforded by the optic vesicle, auditory vesicle, and probably also by the central nervous system, of Osseous Fish. In most Vertebrates these organs are formed as hollow involutions from the exterior; in Osseous Fish, however, as solid involutions, in which a cavity secondarily appears.

The segmental duct of Elasmobranchs or the Wolffian duct (segmental duct) of Birds are cases of a similar kind, being organs which must originally have been formed as hollow involutions, but which now arise as solid bodies.

Only one more instance of this kind need be cited, taken from the Echinoderms.

The body-cavity and the mesoblast investing it arise in the case of most Echinoderms as hollow involutions of the alimentary tract, but in some exceptional groups, Ophiura and Amphiura, are stated to be solid at first and only subsequently to become hollow. Should the accuracy of Metsch-

nikoff's account of this point be confirmed, an almost exact parallel to what has been supposed by me to have occurred with the mesoblast in Elasmobranchs, and other groups, will be supplied.

The tendency of our present knowledge appears to be in favour of regarding the body-cavity in Vertebrates as having been primitively the cavity of alimentary diverticula, and the mesoblast as having formed the walls of the diverticula.

This view, to say the least of it, suits the facts which we know far better than any other theory which has been proposed, and though no doubt the *à priori* difficulties in its way are very great, yet it appears to me to be sufficiently strongly supported to deserve the attention of investigators. In the meantime, however, our knowledge of invertebrate embryology is so new and imperfect that no certainty on a question like that which has just been discussed can be obtained; and any generalizations made at present are not unlikely to be upset by the discovery of fresh facts.

The only other point in connection with the mesoblast which I would call attention to is the formation of the vertebral bodies.

My observations confirm those of Remak and Gegenbaur, shewing that there is a primary segmentation of the vertebral bodies corresponding to that of the muscle-plates, followed by a secondary segmentation in which the central lines of vertebral bodies are opposite the partitions between the muscle-plates.

The explanation of these changes is not difficult to find. The primary segmentation of the body is that of the muscle-plates, which must have been present at a time when the vertebral bodies had no existence. As soon however as the notochordal sheath was required to be strong as well as flexible, it necessarily became divided into a series of segments.

The conditions under which the lateral muscles can cause the flexure of the vertebral column are clearly that each muscle-segment shall be capable of acting on two vertebræ; and this condition can only be fulfilled when the muscle-segments are opposite the intervals between the vertebræ. Owing to this necessity, when the vertebral segments became

formed, their centres corresponded, not with the centres of the muscle-plates, but with the inter-muscular septa.

These considerations fully explain the secondary segmentation of the vertebræ by which they become opposite the inter-muscular septa. On the other hand, the primary segmentation is clearly a remnant of the time when no vertebral bodies were present, and has no greater morphological significance than the fact that the cells to form the unsegmented investment of the notochord were derived from the segmented muscle-plates, and only secondarily became fused into a continuous tube.

The Urino-genital System.

The first traces of the urinary system become visible at about the time of the appearance of the third visceral cleft. At about this period the somatopleure and splanchnopleure become more or less fused together at the level of the dorsal aorta, and thus, as has been already mentioned, each of the original plates of mesoblast becomes divided into a vertebral plate and lateral plate (Pl. v. fig. 6). The mass of cells resulting from this fusion corresponds with Waldeyer's intermediate cell-mass in the Fowl.

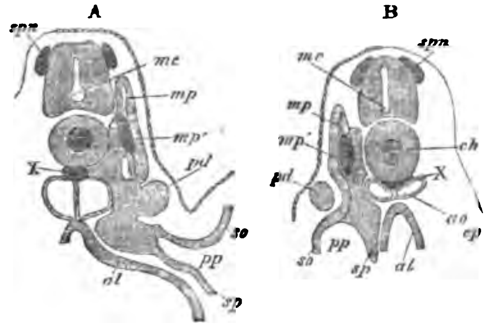
At about the level of fifth protovertebra the first trace of the urinary system appears.

From the intermediate cell-mass a solid knob grows outwards towards the epiblast (woodcut, *pd*). This knob consists at first of 20—30 cells, which agree in character with the neighbouring cells of the intermediate cell-mass, and are at this period rounded. It is mainly, if not entirely, derived from the somatic layer of the mesoblast.

From this knob there grows backwards a solid rod of cells which keeps in very close contact with the epiblast, and rapidly diminishes in size towards its posterior extremity. Its hindermost part consists in section of at most one or two cells. It keeps so close to the epiblast that it might be supposed to be derived from that layer were it not for the sections shewing its origin from the knob above mentioned. We have in this rod the commencement of what I have elsewhere[1] called the segmental duct.

[1] Urinogenital Organs of Vertebrates, *Journ. of Anat. and Phys.* Vol. x.

TWO SECTIONS OF A PRISTIURUS EMBRYO WITH THREE VISCERAL CLEFTS.



The sections are to shew the development of the segmental duct ((*pd*) or primitive duct of the kidneys. In *A* (the anterior of the two sections) this appears as as a solid knob projecting towards the epiblast. In *B* is seen a section of the column which has grown backwards from the knob in *A*.
spn. rudiment of a spinal nerve; *mc.* medullary canal; *ch.* notochord; *X.* string of cells below the notochord; *mp.* muscle-plate; *mp'.* specially developed portion of muscle-plate; *ao.* dorsal aorta; *pd.* segmental duct. *so.* somatopleura; *sp.* splanchnopleura; *pp.* pleuroperitoneal or body-cavity; *ep.* epiblast; *al.* alimentary canal.

My observations show that the segmental duct is developed in the way just described in both Pristiurus and Torpedo. Its origin in Pristiurus is shewn in the adjoining woodcut, and in Torpedo in Plate V. fig. 7*sd.*

At a stage somewhat older than I, the condition of the segmental duct has not very materially altered. It has increased considerably in length, and the knob at its front end is both absolutely smaller, and also consists of fewer cells than before (Pl. V. fig. 7 *sd*). These cells have become more columnar, and have begun to arrange themselves radially; thus indicating the early appearance of the lumen of the duct. The cells forming the front part of the rod, as well as those of the knob, commence to exhibit a columnar character, but in the hinder part of the rod the cells are still rounded. In no part of it has a lumen appeared.

At this period also the knob, partly owing to the commencing separation of the muscle-plate from the remainder of the mesoblast, begins to pass inwards and approach the pleuroperitoneal cavity.

At the same stage the first not very distinct traces of the remainder of the urinary system become developed. These

appear in the form of solid outgrowths from the intermediate cell-mass just at the most dorsal part of the body-cavity.

The outgrowths correspond in numbers with the vertebral segments, and are at first quite disconnected with the segmental duct. At this stage they are only distinctly visible in the first few segments behind the front end of the segmental duct. A full description of them will come more conveniently in the next stage.

By a stage somewhat earlier than K important changes have taken place in the urinary system.

The segmental duct has acquired a lumen in its anterior portion, which opens at its front end into the body-cavity. (Pl. VI. fig. 9 *sd*). The lumen is formed by the columnar cells spoken of in the last stage, acquiring a radiating arrangement round a central point, at which a small hole appears. After the lumen has once become formed, it rapidly increases in size.

The duct has also grown considerably in length, but its hind extremity is still as thin, and lies as close to the epiblast, as at first. The segmental involutions which commenced to be formed in the last stage, have now appeared for every vertebral segment along the whole length of the segmental duct, and even for two or three segments behind this.

They are simple independent outgrowths arising from the outer and uppermost angle of the body-cavity, and are at first almost without a trace of a lumen, though their cells are arranged as two layers. They grow in such a way as to encircle the oviduct on its inner and upper side (Pl. V. fig. 8 and Pl. VI. fig. 14 *b. st*). When the hindermost ones are formed, a slight trace of a lumen is perhaps visible in the front ones. At a stage slightly subsequent to this, in Scyllium Canicula, I noticed 29 of them; the first of them arising in the segment immediately behind the front end of the oviduct (Pl. VI. fig. 17 *st*), and two of them being formed in segments just posterior to the hinder extremity of the oviduct.

Pl. VI. fig. 16 and 18 represent two longitudinal sections showing the segmental nature of the involutions and their relation to the segmental duct.

Many of the points which have been mentioned can be seen by referring to Pl. V. and VI. Anteriorly the segmental

duct opens into the pleuro-peritoneal cavity. In the sections behind this there may be seen the segmental duct with a distinct lumen, and also a pair of segmental involutions (Pl. VI. fig. 14 *a*). In the still posterior sections the segmental duct would be quite without a lumen, and would closely adjoin the epiblast.

It seems not out of place to point out that the modes of the development of the segmental duct and of the segmental involutions are strikingly similar. Both arise as solid involutions, from homologous parts of the mesoblast. The segmental duct arises in the vertebral segment immediately in front of that in which the first segmental involution appears; *so that the segmental duct appears to be equivalent to a single segmental involution.*

The next stage corresponds with the first appearance of the external gills. The segmental duct now communicates by a wide opening with the pleuro-peritoneal cavity (Pl. VI. fig. 9 *sd*). It possesses a lumen along its whole length up to the extreme hind end (Pl. VI. fig. 9 *a*). It is, however, at this hinder extremity that the most important change has taken place. This end has grown downwards towards that part of the alimentary canal which still lies behind the anus. This downgrowth is beginning to show distinct traces of a lumen, and will appear in the next stage as one of the horns by which the segmental ducts communicate with the cloaca (Pl. VI. fig. 9 *b*). All the anterior segmental involutions have now acquired a lumen. But this is still absent in the posterior ones (Pl. VI. fig. 9 *a*).

Owing to the disappearance of the body-cavity in the region behind the anus, the primitive involutions there remain as simple masses of cells still disconnected with the segmental duct (Pl. VI. fig. 9 *b*, 9 *c* and 9 *d*).

Primitive Ova. The true generative products make their first appearance as the *primitive ova* between stages I and K.

In the sections of one of my embryos of this stage they are especially well shown, and the following description is taken from those displayed in that embryo.

They are confined to the region which extends posteriorly nearly to the end of the small intestine and anteriorly to the abdominal opening of the segmental duct.

Their situation in this region is peculiar. There is no trace of a distinct genital ridge, but the ova mainly lie in the dorsal

portion of the mesentery, and therefore in a part of the mesoblast which distinctly belongs to the splanchnopleure (Pl. VI. fig. 14*a*). Some are situated external to the segmental involutions; and others again, though this is not common, in a part of the mesoblast which distinctly belongs to the body-wall (Pl. VI. fig. 14 *b*).

The portion of mesentery in which the primitive ova are most densely aggregated, corresponds to the future position of the genital ridge, but the other positions occupied by ova are quite outside this. Some ova are in fact situated on the outside of the segmental duct and segmented tubes, and must therefore effect a considerable migration before reaching their final positions in the genital ridge on the inner side of the segmental duct (Pl. VI. fig. 14 *b*).

The condition of the tissue in which the ova appear may at once be gathered from an examination of the figures given. It consists of an irregular epithelium of cells partly belonging to the somatopleure and partly to the splanchnopleure, but passing uninterruptedly from one layer to the other. The cells which compose it are irregular in shape, but frequently columnar (Pl. VI. fig. 14 *a* and 14 *b*).

They are formed of a nucleus which stains deeply, invested by a *very delicate* layer of protoplasm. At the junction of somatopleure and splanchnopleure they are more rounded than elsewhere. Very few loose connective-tissue cells are present. The cells just described vary from ·008 Mm. to ·01 Mm. in diameter.

The primitive ova are situated amongst them and stand out with extraordinary clearness, to which justice is hardly done in my figures.

The normal full-sized ova exhibit the following structure. They consist of a mass of somewhat granular protoplasm of irregular, but more or less rounded, form. Their size varies from ·016—·036 Mm. In their interior a nucleus is present, which varies from ·012—·016 Mm., but its size as a rule bears *no* relation to the size of the containing cell.

This is illustrated by the subjoined list of measurements.

The numbers given refer to degrees on my micrometer scale.

Since it is the ratio alone which it is necessary to call attention to, the numbers are not reduced to decimals of a millimeter. Each degree of my scale is equal, however, with the object glass employed, to ·002 Mm.

Size of Primitive ova in degrees of micrometer scale with F. ocul 2.	Size of nucleus of Primitive ova in degrees of micrometer scale with F. ocul 2.
10	8
13	8
13	8
14	7
15	7
13	7½
11	8
16	5½
12	7
10	7
15	6
13	6
12	7

This series brings out the result I have just mentioned with great clearness.

In one case we find a cell has three times the diameter of the nucleus 16 : 5½; in another case 10 : 8, the nucleus has only a slightly smaller diameter than the cell. The irrationality of the ratio is fairly shewn in some of my figures, though none of the largest cells with very small nuclei have been represented.

The nuclei are granular, and stain fairly well with hæmatoxylin. They usually contain a single deeply stained nucleolus, but in many cases, especially where large (and this independently of the size of the cell), they contain two nucleoli (Pl. VI. fig. 14 *c* and 14 *d*), and are at times so lobed as to give an apparent indication of commencing division.

A multi-nucleolar condition of the nuclei, like that figured by Götte[1], does not appear till near the close of embryonic life, and is then found equally in the large ova and in those not larger than the ova which exist at this early date.

As regards the relation of the primitive ova to each other and the neighbouring cells, there are a few points which deserve attention. In the first place, the ova are, as a rule, collected in masses at particular points, and not distributed uniformly (fig. 14. *a*.) The masses in some cases appear as if they had

[1] *Entwicklungsgeschichte der Unke*, Pl. I. fig. 8.

resulted from the division of one primitive ovum, but can hardly be adduced as instances of a commencing coalescence; since if the ova thus aggregated were to coalesce, an ovum would be produced of a very much greater size than any which is found during the early stages. Though at this stage no indication is present of such a coalescence of cells to form ova as is believed to take place by Götte, still the origin of the primitive ova is not quite clear. One would naturally expect to find a great number of cells intermediate between primitive ova and ordinary columnar cells. Cells which may be intermediate are no doubt found, but not nearly so frequently as might have been anticipated. One or two cells are shewn in Pl. VI. fig. 14 *a*. *x*, which are perhaps of an intermediate character; but in most sections it is not possible to satisfy oneself that any such intermediate cells are present.

In one case what appeared to be an intermediate cell was measured, and presented a diameter of ·012 Mm. while its nucleus was ·008 Mm. Apart from certain features of the nucleus, which at this stage are hardly very marked, the easiest method of distinguishing a primitive ovum from an adjacent cell is the presence of a large quantity of protoplasm around the nucleus. The nucleus of one of the smallest primitive ova is not larger than the nucleus of an ordinary cell (being about ·008 Mm. in both). It is perhaps the similarity in the size of the nuclei which renders it difficult at first to distinguish developing primitive ova from ordinary cells. Except with the very thinnest sections a small extra quantity of protoplasm around a nucleus might easily escape detection, and the developing cell might only become visible when it had attained to the size of a small typical primitive ovum.

It deserves to be noticed that the nuclei even of some of the largest primitive ova scarcely exceed the surrounding nuclei in size. This appears to me to be an argument of some weight in shewing that the great size of primitive ova is not due to the fact of their having been formed by a coalescence of different cells (in which case the nucleus would have increased in the same proportion as the cell); but to an increase by a normal method of growth in the protoplasm around the nucleus.

It appears to me to be a point of great importance certainly to determine whether the primitive ova arise by a meta-

morphosis of adjoining cells, or may not be introduced from elsewhere. In some of the lower animals, *e. g.* Hydrozoa, there is no question that the ova are derived from the epiblast; we might therefore expect to find that they had the same origin in Vertebrates. Further than this, ova are frequently capable in a young state of executing amœboid movements, and accordingly of migrating from one layer to another. In the Elasmobranchs the primitive ova exhibit in a hardened state an irregular form which might appear to indicate that they possess a power of altering their shape, a view which is further supported by some of them being at the present stage situated in a position very different from that which they eventually occupy, and which they can only reach by migration. If it could be shewn that there were no intermediate stages between the primitive ova and the adjoining cells (their migratory powers being admitted) a strong presumption would be offered in favour of their having migrated from elsewhere to their present position. In view of this possibility I have made some special investigations, which have however led to no very satisfactory results. There are to be seen in the stages immediately preceding the present one, numerous cells in a corresponding position to that of the primitive ova, which might very well be intermediate between the primitive ova and ordinary cells, but which offer no sufficiently well marked features for a certain determination of their true nature.

In the particular embryo whose primitive ova have been described these bodies were more conspicuous than in the majority of cases, but at the same time they presented no special or peculiar characters.

In a somewhat older embryo of Scyllium the cells amongst which the primitive ova lay had become very distinctly differentiated as an epithelium (the germinal epithelium of Waldeyer) well separated by what might almost be called a basement membrane from the adjoining connective-tissue cells. Hardly any indication of a germinal ridge had appeared, but the ova were more definitely confined than in previous embryos to the restricted area which eventually forms this. The ova on the average were somewhat smaller than in the previous cases.

In several embryos intermediate in age between the embry-

whose primitive ova were described at the commencement of this section and the embryo last described, the primitive ova presented some peculiarities, about the meaning of which I am not quite clear, but which may perhaps throw some light on the origin of these bodies.

Instead of the protoplasm around the nucleus being clear or slightly granular, as in the cases just described, it was filled in the most typical instances with numerous highly refracting bodies resembling yolk-spherules. In osmic acid specimens (Pl. VI. fig. 15) these stain very darkly, and it is then as a rule very difficult to see the nucleus; in specimens hardened in picric acid and stained with hæmatoxylin these bodies are stained of a deep purple colour, but the nucleus can in most cases be distinctly seen. In addition to the instances in which the protoplasm of the ova is quite filled with these bodies, there are others in which they only occupy a small area adjoining the nucleus (Pl. VI. fig. 15 *a*), and finally some in which only one or two of these bodies are present. The protoplasm of the primitive ova appears in fact to present a series of gradations between a state in which it is completely filled with highly refracting spherules and one in which these are completely absent.

This state of things naturally leads to the view that the primitive ova, when they are first formed, are filled with these spherules, which are probably yolk-spherules, but that they gradually lose them in the course of development. Against this interpretation is the fact that the primitive ova in the younger embryo first described are completely without these bodies; this embryo however unquestionably presented an abnormally early development of the ova; and I am satisfied that embryos present considerable variations in this respect.

If the primitive ova are in reality in the first instance filled with yolk-spherules, the question arises as to whether, considering that they are the only mesoblast cells filled at this period with yolk-spherules, we must not suppose that they have migrated from some peripheral part of the blastoderm into their present position. To this question I can give no satisfactory answer. Against a view which would regard the spherules in the protoplasm as bodies which appear subsequently to the first formation of the ova, is the fact that hitherto

no instances in which these spherules were present have been met with in the later stages of development after the appearance of the external gills; and they seem therefore to be confined to the first stages.

Notochord.

The changes undergone by the notochord during this period present considerable differences according to the genus examined. One type of development is characteristic of Scyllium and Pristiurus; a second type, of Torpedo.

My observations being far more complete for Scyllium and Pristiurus than for Torpedo, it is to the two former genera only that the following account applies, unless the contrary is expressly stated. Only the development of the parts of the notochord in the trunk are here dealt with; the cephalic section of the notochord is treated of in a subsequent section.

During stage G the notochord is composed of flattened cells arranged vertically, rendering the histological characters of the notochord difficult to determine in transverse sections. In longitudinal sections, however, the form and arrangement of the cells can be recognised with great ease. At the beginning of stage G each cell is composed of a nucleus invested by granular protoplasm frequently vacuolated and containing in suspension numerous yolk-spherules. It is difficult to determine whether there is only one vacuole for each cell, or whether in some cases there may not be more than one.

Round the exterior of the notochord there is present a distinct though delicate cuticular sheath.

The vacuoles are at first small, but during stage G rapidly increase in size, while at the same time the yolk-spherules completely vanish from the notochord.

As a result of the rapid growth of the vacuoles, the nuclei, surrounded in each case by a small amount of protoplasm, become pushed to the centre of the notochord, the remainder of the protoplasm being carried to the edge. The notochord thus becomes composed during stages H and I (Pl. v. fig. 4—6) of a central area mainly formed of nuclei with a small quantity of protoplasm around them, and of a thin peripheral layer of protoplasm without nuclei, the widish space between the two being filled with clear fluid. The exterior of the cells is

indurated, so that they may be said to be invested by a membrane; the cells themselves have a flattened form, and each extends from the edge to the centre of the notochord, the long axis of each being rather greater than half the diameter of the cord.

The nuclei of the notochord are elliptical vesicles, consisting of a membrane filled with granular contents, amongst which is situated a distinct nucleolus. They stain deeply with hæmatoxylin. Their long diameter in Scyllium is about 0·02 Mm.

The diameter of the whole notochord in Pristiurus during stage I is about 0·1 Mm. in the region of the back, and about 0·08 Mm. near the posterior end of the body.

Owing to the form of its constituent cells, the notochord presents in transverse sections a dark central area surrounded by a lighter peripheral one, but its true structure cannot be unravelled without the assistance of longitudinal sections. In these (Pl. VI. fig. 10) the nuclei form an irregular double row in the centre of the cord. Their outlines are very clear, but those of the individual cells cannot for certain be made out. It is, however, easy to see that the cells have a flattened and wedge-shaped form, with the narrow ends overlapping and interlocking at the centre of the notochord.

By the close of stage I the cuticular sheath of the notochord has greatly increased in thickness.

During the period intermediate between stages I and K the notochord undergoes considerable transformations. Its cells cease to be flattened, and become irregularly polygonal, and appear but slightly more compressed in longitudinal sections than in transverse ones. The vacuolation of the cells proceeds rapidly, and there is left in each cell only a very thin layer of protoplasm around the nucleus. Each cell, as in the earlier stages, is bounded by a membrane-like wall.

Accompanying these general changes special alterations take place in the distribution of the nuclei and the protoplasm. The nuclei, accompanied by protoplasm, gradually leave the centre and migrate towards the periphery of the notochord. At the same time the protoplasm of the cells forms a special layer in contact with the investing sheath.

The changes by which this takes place can easily be followed in longitudinal sections. In Pl. VI. fig. 11 the migration of the nuclei has commenced. They are still, however, more or less

aggregated at the centre, and very little protoplasm is present at the edges of the notochord. The cells, though more or less irregularly polygonal, are still somewhat flattened. In Pl. VI. fig. 12 the notochord has made a further progress. The nuclei now mainly lie at the side of the notochord, where they exist in a somewhat shrivelled state, though still invested by a layer of protoplasm.

A large portion of the protoplasm of the cord forms an almost continuous layer in close contact with the sheath, which is more distinctly visible in some cases than in others.

While the changes above described are taking place the notochord increases in size. At the age of fig. 11 it is in the anterior part of the body of Pristiurus about 0·11 Mm. At the age of fig. 12 it is in the same species 0·12 Mm., while in Scyllium Stellare it reaches about 0·17 Mm.

During stage K (Pl. V. fig. 8) the vacuolation of the cells of the notochord becomes even more complete than during the earlier stages, and in the central cells hardly any protoplasm is present, though a starved nucleus surrounded by a little protoplasm may be found in an occasional corner.

The whole notochord becomes very delicate, and can with great difficulty be conserved whole in transverse sections.

The layer of protoplasm which appeared during the last stage on the inner side of the cuticular membrane of the notochord becomes during the present stage a far thicker and more definite structure. It forms a continuous layer with irregular prominences on its inner surface; and contains numerous nuclei. The layer sometimes presents in transverse sections hardly any indication of a division into a number of separate cells, but in longitudinal sections this is generally very obvious. The cells are directed very obliquely forwards, and consist of an oblong nucleus invested by protoplasm. The layer formed by them is very delicate and very easily destroyed. In one example its thickness varied from ·004 to ·006 Mm., in another it reached ·012 Mm. The thickness of the cuticular membrane is about ·002 Mm. or rather less.

The diameter of a notochord in the anterior part of the body of a Pristiurus embryo of this stage is about 0·21 Mm. Round the exterior of the notochord the mesoblast cells are commencing to arrange themselves as a special sheath.

In Torpedo the notochord at first presents the same structure as in Pristiurus, *i.e.* it forms a cylindrical rod of flattened cells.

The vacuolation of these cells does not however commence till a relatively very much later period than in Pristiurus, and also presents a very different character (Pl. v. fig. 7).

The vacuoles are smaller, more numerous, and more rounded than in the other genera, and there can be no question that in many cases there is more than one vacuole in a cell. The most striking point in which the notochord of Torpedo differs from that of Pristiurus consists in the fact that in Torpedo there is never any aggregation of the nuclei at the centre of the cord, but the nuclei are always distributed uniformly through it. As the vacuolation proceeds the differences between Torpedo and the other genera become less and less marked. The vacuoles become angular in form, and the cells of the cord cease to be flattened, and become polygonal.

At my final stage for Torpedo (slightly younger than K) the only important feature distinguishing the notochord from that of Pristiurus, is the absence of any signs of nuclei or protoplasm passing to the periphery. Around the exterior of the cord there is early found in Torpedo a special investment of mesoblastic cells.

EXPLANATION OF PLATE V.

Complete list of reference letters.

ep. epiblast. *df.* dorsal fin. *sp. c.* spinal cord.
w. white matter of spinal cord. *nc.* neural canal.
pr. posterior root of spinal nerve.
ar. anterior root of spinal nerve. *mp.* muscle-plate.
mp'. early formed band of muscles from the splanchnic layer of the muscle-plates.
Vr. vertebral rudiment. *so.* somatic layer of mesoblast.
sp. splanchnic layer of mesoblast. *pp.* body-cavity.
pc. pericardial cavity. *c.* connective-tissue cells.
sd. segmental duct. *st.* segmental tube. *po.* primitive ovum.
ao. dorsal aorta. *ca v.* cardinal vein. *sv.* sinus venosus.
ht. heart. *v.* splanchnic vein. *ch.* notochord.
x. subnotochordal rod. *al.* alimentary tract. *sp. v.* spiral valve.
y. passage connecting the neural and alimentary canals.
l. liver. *p.* protoplasm from yolk in the alimentary tract.

Fig. 1. Section from the caudal region of a Pristiurus embryo belonging to stage H. Zeiss C. Ocul. 1. Osmic acid specimen.

It shews (1) the constriction of the subnotochordal rod (*x*) from the summit of the alimentary canal. (2) The formation of the body-cavity in the muscle-plate and the ventral thickening of the parietal plate.

Fig. 1*a*. Portion of alimentary wall of the same embryo, shewing the formation of the subnotochord rod (*x*).

Fig. 2. Section through the caudal vesicle of a Pristiurus embryo belonging to stage H. Zeiss C. Ocul. 1.

It shews the bilobed condition of the alimentary vesicle and the fusion of the mesoblast and hypoblast at the caudal vesicle.

Fig. 3*a*. Sections from the caudal region of a Pristiurus embryo belonging to stage H. Zeiss C. Ocul. 1. Picric acid specimen.

It shews the communication which exists posteriorly between the neural and alimentary canals, and also by comparison with 3*b* it exhibits the dilatation undergone by the alimentary canal in the caudal vesicle.

Fig. 3*b*. Section from the caudal region of an embryo slightly younger than 3*a*. Zeiss C. Ocul. 1. Osmic acid specimen.

Fig. 4. Section from the cardiac region of a Pristiurus embryo belonging to stage H. Zeiss C. Ocul. 1. Osmic acid specimen.

It shews the formation of the heart (*ht*) as a cavity between the splanchnopleure and the wall of the throat.

Fig. 5. Section from the posterior dorsal region of a Scyllium embryo, belonging to stage H. Zeiss C. Ocul. 1. Osmic acid specimen.

It shews the general features of an embryo of stage H, more especially the relations of the body-cavity in the parietal and vertebral portions of the lateral plate, and the early formed band of muscle (*mp'*) in the splanchnic layer of the vertebral plate.

Fig. 6. Section from the œsophageal region of Scyllium embryo belonging to stage I. Zeiss C. Ocul. 1. Chromic acid specimen.

It shews the formation of the rudiments of the posterior nerve-roots (*pr*) and of the vertebral rudiments (*Vr*).

Fig. 7. Section of a Torpedo embryo belonging to stage slightly later than I. Zeiss C. Ocul. 1. reduced $\frac{1}{3}$. Osmic acid specimen.

It shews (1) the formation of the anterior and posterior nerve-roots. (2) The solid knob from which the segmental duct (*sd*) originates.

Fig. 8. Section from the dorsal region of a Scyllium embryo belonging to a stage intermediate between I and K. Zeiss C. Ocul. I. Chromic acid specimen.

It illustrates the structure of the primitive ova, segmental tubes, notochord, etc.

Fig. 8*a*. Section from the caudal region of an embryo of the same age as 8. Zeiss A. Ocul. 1.

It shews (1) the solid œsophagus. (2) The narrow passage connecting the pericardial and body cavities.

EXPLANATION OF PLATE VI.

Complete list of reference letters.

ep. epiblast. *sp. c.* spinal canal.
pr. rudiment of posterior root of spinal nerve.
ar. " " anterior root of spinal nerve.
b. anterior fin. *mp.* muscle-plate.
mp'. early formed band of muscles. *Vr.* vertebral rudiment.
pp. body-cavity. *um.* umbilical cord. *sd.* segmental duct.
st. segmental tube. *sr.* supra-renal body. *po.* primitive ovum.
ge. germinal epithelium. *vc.* visceral cleft. *ao.* dorsal aorta.
ca v. cardinal vein. *v.* splanchnic vein.
ua. umbilical artery. *uv.* umbilical vein.
v. blood-vessel. *ch.* notochord.
sh. cuticular sheath of notochord. *x.* subnotochordal rod.
al. alimentary tract. *l.* liver.
an. point where anus will be formed.

Fig. 9. Section of a Pristiurus embryo belonging to stage K. Zeiss A. Ocul. 1. Osmic acid specimen.

It shews the formation of the liver (*l*), the structure of the anterior fins (*b*), and the anterior opening of the segmental duct into the body-cavity (*sd*).

Fig. 9*a*, 9*b*, 9*c*, 9*d*. Four sections through the anterior region of the same embryo as 9. Osmic acid specimens.

The sections shew (1) the atrophy of the post-anal section of the alimentary tract (9*b*, 9*c*, 9*d*). (2) The existence of the segmental tubes behind the anus (9*b*, 9*c*, 9*d*). With reference to these it deserves to be noted that the segmental tubes behind the anus are quite disconnected, as is proved by the fact that a tube is absent on one side in 9*c* but reappears in 9*d*. (3) The downward prolongation of the segmental duct to join the posterior extremity of the alimentary tract (9*b*).

Fig. 10. Longitudinal and horizontal section of a Scyllium embryo of stage H. Zeiss C. Ocul. 1. Reduced by $\frac{1}{3}$. Picric acid specimen.

It shews (1) the structure of the notochord; (2) the appearance of the early formed band of muscles (*mp'*.) in the splanchnic layer of the protovertebra.

Fig. 11. Longitudinal and horizontal sections of an embryo belonging to stage I. Zeiss C. Ocul. 1. Chromic acid specimen. It illustrates the same points as the previous section, but in addition shews the formation of the rudiments of the vertebral bodies (*Vr*) which are seen to have the same segmentation as the muscle-plates.

Fig. 12. Longitudinal and horizontal section of an embryo belonging to the stage intermediate between I and K. Zeiss C. Ocul. 1. Osmic acid specimen illustrating the same points as the previous section.

Fig. 13. Longitudinal and horizontal section of an embryo belonging to stage K, Zeiss C. Ocul. 1, and illustrating same points as previous section.

Fig. 14*a*, 14*b*, 14*c*, 14*d*. Figures taken from preparations of an embryo of an age intermediate between I and K, and illustrating the structure of the primitive ova. Fig. 14*a* and 14*b* are portions of sections Zeiss C. Ocul. 3 reduced $\frac{1}{3}$. Fig. 14*c* and 14*d* are individual ova, shewing the commencing division of nucleus. Zeiss F. Ocul. 2.

Fig. 15. Osmic acid preparation of primitive ova belonging to stage K Zeiss immersion No. 2, Ocul. 1. The protoplasm of the ova is seen to be nearly filled with bodies resembling yolk-spherules: and one ovum is apparently undergoing division.

Fig. 15*a*. Picric acid preparation shewing a primitive ovum partially filled with bodies resembling yolk-spherules.

Fig. 16. Horizontal and longitudinal section of Scyllium embryo belonging to stage K. Zeiss A. Ocul. 1. Picric acid preparation. The connective-tissue cells are omitted.

The section shews that there is one segmental tube to each vertebral segment.

Fig. 17. Portion of a Scyllium embryo belonging to stage K, viewed as a transparent object.

It shews the segmental duct and the segmental involutions—two of which are seen to belong to segments behind the end of the alimentary tracts.

Fig. 18. Vertical longitudinal section of a Scyllium embryo belonging to stage K. Zeiss A. Ocul. 1. Hardened in a mixture of osmic and chromic acids. It shews

(1) the commissures connecting together the posterior roots of the spinal nerves;
(2) the junction of the anterior and posterior roots;
(3) the relations of the segmental ducts to the segmental involutions;
(4) the germinal epithelium lining the body-cavity.

THE ACTION OF PILOCARPIN ON THE SUB-MAXILLARY GLAND OF THE DOG. By J. N. LANGLEY, B.A., *St John's College, Cambridge.*

(*From the Physiological Laboratory, Cambridge.*)

IT has for some time been well known that jaborandi causes in man and the higher vertebrates a very marked salivary secretion. It might then not unnaturally be supposed, that an inquiry into its method of action would possibly suggest some more complete explanation than we have at present of the salivary secretion, and so of secretion in general. The following experiments were begun with that end in view; but the experiments necessary to verify the suggestions offered, have proved so many and varied, that I venture in the meanwhile to describe the action of the poison on the salivary glands, leaving a discussion of the rationale of secretion to a future paper.

The necessity of using the inconvenient aqueous and alcoholic extracts of jaborandi has of late been obviated by the separation of its alkaloid pilocarpin. In these experiments I have used the nitrate of pilocarpin [1], a salt of the alkaloid very readily soluble in water.

The sub-maxillary gland of the dog was chosen for experi-

[1] I have, throughout, obtained it from Mr Martindale.

ment, owing to its exposed condition and to the comparative ease with which its nerves can be isolated; a few experiments were made on the parotid, but these were not increased in number, since there seems little reason to doubt that that which is true for one salivary gland is also with slight modifications true for the rest.

In every case the animal was placed under anæsthetics during the operation and killed at its close; the anæsthetics employed have been various, most frequently morphia or chloroform, occasionally chloral hydrate, or croton chloral hydrate.

In registering the amount of salivary secretion and of the blood-flow through the gland, a Ludwig's kymograph was used, against the slowly-moving paper of which lightly pressed three levers, in the same vertical line, each attached to the crosspiece of an electro-magnet, the lower one arranged in the usual way to mark seconds, the other two connected with a key and galvanic cell, so that when the key was put down a mark was made on the paper; one of the upper levers was used to register the amount of saliva, and the other the blood-flow, each key being put down for a definite quantity of fluid. In the case of the saliva a cannula tied in Wharton's duct was connected by a T piece with a tube divided into a number of equal parts; tubes of different calibre were used according to the nature of the experiment or at different stages of the experiment, so that the divisions, in all of about equal length, contained 1-8, 1-10, or 1-32 of a cubic centimetre. In observing the flow of blood, all the veins going to the jugular were tied, except the veins coming from the gland; then either the jugular was tied and cut across on the peripheral side of the ligature and the blood allowed to run into a narrow test-tube, of which each division was equal to ·5 cc; or a cut was made just at the division of the jugular, the jugular itself clamped, and the blood collected as before; in the latter case, when it was not necessary to record the blood-flow, a clamp was arranged so as just to pinch up the cut, and the clamp on the jugular taken off; in this way the blood returned to the heart and unnecessary loss was avoided.

By means of one of the keys the beginning and end of the

stimulation of a nerve, or of the injection of any substance, could also be recorded.

Occasionally the crural artery was connected with a manometer in the usual way, to be able to eliminate any effect from varying blood-pressure.

The pilocarpin was injected sometimes into the saphena vein and sometimes through the facial artery direct into the gland, in the manner described by Heidenhain (*Pflüger's Archiv*, Band v.), except that the subclavian arteries were not tied.

In every case the stimulus used was a Daniell's cell with a Du Bois Reymond's induction apparatus; with this the current was just perceptible to the tongue, when the secondary coil was at 12 or 13.

The effects of pilocarpin are, as will be seen, very different according to the amount of the dose.

A small quantity injected into the saphena vein causes in about thirty seconds a secretion of saliva and an increased flow of blood; both begin at about the same time, rapidly reaching a maximum, which is maintained for a varying short time; and both then decline slowly, and, as the secretion becomes less, still more slowly, so that it may be twenty, thirty, or more minutes before the normal condition of things is arrived at.

The minimum amount of pilocarpin which will produce secretion is very small, a few milligrams injected into the gland artery causing a marked flow of saliva.

The secretion is not affected by section of either the chorda tympani or the sympathetic nerve.

Stimulation of the peripheral end of the chorda tympani with currents of medium strength, gives an increase of secretion at whatever stage of the secretion it be stimulated. In one case, however, which certainly is not normal, a diminution of the flow was repeatedly caused by chorda tympani stimulation; the cause of this at present I can but guess at. Sometimes with rather strong currents the effect of chorda tympani stimulation was almost exactly that which would have been produced, had the poison not been acting, so that instead of adding its normal effects to those of the pilocarpin it merely increased those effects up to the normal stimulation amount. An experiment will shew this more clearly:

		Blood flow per minute 1° = ½ c.c.	Saliva flow per minute 1° = ⅛ c.c.
5·3	Normal	5°	—
5·5	Stimulated ch. ty. for 40″ sec. coil 11	rate 27°	12°
5·29	... ...	4°	—
5·30	Injected into facial artery towards the gland (not stopping the blood-supply) 6 minims of a 5 p.c. sol. pilocarpin. The blood and saliva flow are influenced almost immediately, the former reaching its maximum rapidity in 20″, the latter in 30″	rate 22°	10°
5·40	... ...	10°	3°
5·42	Stimulated ch. ty. for 25″ sec. coil 11 ...	rate 27°	10°
5·45	... ...	8°	1°
5·47	Stimulated ch. ty. for 25″ sec. coil 11	rate 27°	8°

The above also shews the powerful effect that pilocarpin has on the gland; 17 mgrs. producing almost as great an effect as stimulation of the chorda tympani with the fairly strong current produced when the secondary coil is at 11.

Stimulation of the sympathetic during the increased flow by pilocarpin causes a slowing of the blood-flow and of the secretion, but I have not been able to stop the secretion by this means; the slowing probably depends on the lessened blood-supply.

The latent period of secretion with pilocarpin varies directly with the amount injected, just as it does with weak or strong chorda tympani stimulation.

If a second small quantity of pilocarpin be injected, the same results will follow as before, but unless some time has elapsed the effect is rather less in degree. The injection may be repeated several times with even feebler results, until a condition is reached in which there is a very slow continuous secre-

tion with a sub-normal blood-flow, and in which stimulation of the chorda tympani with whatever strength of current produces very slight effects on the saliva and comparatively slight on the blood-flow. But since before this stage has been reached, the pilocarpin has caused a very considerable fall of blood-pressure, and a weakening as well as a slowing of the heart, it is better to adopt another method of experiment, which will avoid as much as possible these sources of error, to see the effect of large doses. This may be done by injecting into the gland artery by Heidenhain's method, and operating in addition to observe the blood-flow, so that a great part of the pilocarpin may run out of the body[1].

Suppose that under such circumstances ·1 gm. of pilocarpin be injected, there will be for a short time, a minute or so, a rapid secretion, which rapidly will decline, so that in a few seconds later there will be a very slow secretion, perhaps of 1-32 cc. in two to three minutes, with a scanty blood-flow; stimulation of the chorda tympani will increase the secretion to perhaps 1-32 cc. in one minute, and produce a marked but comparatively slight increase in the blood-flow: subsequently the secretion becomes slower and slower, so that perhaps there is but 1-32 cc. saliva in five to ten minutes; which is unaltered by stimulation of the chorda tympani: finally the secretion stops altogether, and there is barely any blood-flow through the gland. Stimulation of the sympathetic still produces a secretion.

If now the animal be left a varying time the secretion starts again very slowly, but stimulation of the chorda tympani produces no effect; the flow slightly increases and the chorda tympani becomes faintly irritable, so that the saliva and the blood-flow are both increased, especially the latter, by stimulation of the nerve; these effects gradually become more marked until there is a fair secretion and fair nerve irritability.

We have seen that pilocarpin in not too large quantity produces just those effects which are produced by stimulating

[1] Even under these conditions it sometimes occurs that sufficient pilocarpin is carried to the heart to cause it to stop completely. If this appear imminent, the animal may be kept alive for some other experiment suggested by the circumstances by injecting 15 to 20 mgm. of atropin into a vein; the injection of atropin must not be deferred too long, or it will be useless.

the chorda tympani; we might therefore expect that after atropin has been given the effects of injecting a not too large quantity of pilocarpin would be similar to those of chorda tympani stimulation; this indeed is the case. It is well known that after atropin has been given stimulation of the chorda tympani causes an increase of blood-flow, but no longer a secretion of saliva; injection of pilocarpin into a vein at this stage gives an increase of blood-flow, but no secretion of saliva. This as a general statement is true, yet the matter is not quite so simple as might appear from such a statement, for when the chorda tympani is paralysed by atropin the increase of blood-flow from pilocarpin is very much less than that which would normally have been produced. This is, I believe, in part intimately connected with the fact that the increase of blood-flow by the injection of pilocarpin in such circumstances is generally less than that from chorda tympani stimulation, and in part is dependent upon the action of atropin. The effect of atropin on the vaso-dilator fibres of the chorda tympani has, I think, been rather underrated; in several experiments the following has been the course of events: on injecting a small quantity of atropin sulphate, say 5 mgr., the secretory power of the chorda tympani is lowered in the most marked manner, with little if any change in the vaso-dilator effects; on a further injection of say 2 mgr. the saliva rises slightly in fairly strong stimulation (sec. coil 10), the blood flowing rapidly but less than before. Although such a very striking diminution of the secretory effect of the chorda tympani is produced by the injection of 7 mgr. of atropin, yet to get rid of this small remaining effect atropin has to be injected to 10-16 mgr. The last doses of atropin produce an effect on the vaso-dilator fibres, so that when no secretion follows stimulation of the chorda tympani for 1′ 30″ with coil 8, the blood-flow, though strikingly increased, is much less than that normally produced.

It is this, I think, which largely causes the marked diminution in increase of blood-flow by pilocarpin after atropin.

It has been shown by Vulpian and others that atropin stops the salivary secretion which has been started by pilocarpin; this is easily verified, moreover the quantity required is relatively small, but the quantity required to paralyse the chorda

tympani when pilocarpin in small doses has been given is larger than that normally required, and so up to a certain point the greater the amount of pilocarpin given, the greater the amount of atropin necessary to paralyse the chorda tympani.

Vulpian has also stated[1] that after atropin has paralysed the chorda tympani, pilocarpin can cause no salivary secretion. With the heart of the frog[2] I have shown that atropin and jaborandi exert an action depending on their relative proportions, and that a heart freed from jaborandi stand-still by atropin can again be brought to a stand-still by jaborandi, and once more freed from it by atropin. A corresponding state of things holds good with the salivary gland: the pilocarpin secretion that has been stopped by atropin can be renewed by pilocarpin and again stopped by atropin; this may be proved by injecting into a vein, but is much more satisfactorily shown by injecting into the gland artery by the facial and allowing the first blood to flow out by the jugular. The following experiments will illustrate this antagonistic action:

		Saliva flow.
11.40.	Stimulated ch. ty. for 12 seconds. Sec. coil 11.	3° in 12″, *i.e.* rate 15° in 60″.
11.50.	Injected into saphena vein 17 mgm. atropin.	
12.0.	Stimulated ch. ty. Sec. coil 10 for 1 minute.	No trace.
12.25.	Stimulated ch. ty. Sec. coil 8 for 1 minute.	No trace.
12.30.	Injected into facial artery towards gland ·1 grm. pilocarpin. In 10 to 20 seconds the saliva begins to flow.	5° in 60″.
1.0.	Injected into saphena vein 20 mgrm. atropin.	stopped almost immediately.

1.15. Stimulated ch. ty. Good secretion.
1.17. Injected 43 mgr. pilocarpin into gland by artery. Almost immediately a rapid secretion, which rapidly becomes slow.
1.20. Injected into saphena vein 20 mgr. atropin. Secretion stopped.
1.25. Stimulated ch. ty. Sec. coil 9 for 1 minute. No trace of secretion.
1.35. Both ch. ty. still paralysed.

[1] Quoted by Nicolini, *Hist. des Pilocarpus*, 1876.
[2] *Journal of Anat. and Phys.* Oct. 1875.

1.40. Injected into gland by artery ·1 grm. pilocarpin. In about one minute secretion begins.
1.45. Saliva flow 2° in 40″.
1.46. Stimulated ch. ty. for 28″. Sec. coil 10. 2° in 28″.
2.10. Secretion stopped; both ch. ty. paralyzed, *i.e.* the pilocarpin has been washed out of the body, escaping by the jugular, so that the atropin remaining in the blood for the second time caused paralysis.

Summing up then the action of pilocarpin:

In *small doses, i.e.* up to about 30 mgr. It exerts an action on the gland very similar to that produced by stimulation of the chorda tympani.

It causes a rapid secretion, and a considerable increase of blood-flow; both secretion and blood-flow gradually declining.

Its effects are little if at all altered by section of the chorda tympani or of the sympathetic nerve.

Stimulation of the chorda tympani increases the pilocarpin effects, *i.e.* the nerve is functionally unaltered.

Stimulation of the sympathetic diminishes its effects, so that this nerve too is functionally unaltered.

The secretion is stopped by injecting atropin (a fact for some time known), but a quantity of atropin sufficient to paralyse the chorda tympani does *not* prevent a relatively large quantity of pilocarpin from producing its ordinary results. In fact, the secretion or absence of secretion is dependent on the relative quantity of the two poisons present, just as is the stand-still or beat of the heart.

In *larger doses.* Instead of causing a stronger saliva-flow, it causes none at all[1], and further prevents the chorda tympani from producing any secretion.

It considerably diminishes the blood-flow through the gland, as well as the effect of the chorda tympani on the blood-flow.

It does not however stop the sympathetic secretion. The action indeed is not very dissimilar to that of atropin; this agrees with its action on the vagus and inhibitory apparatus of the heart (*loc. cit.*), where in large doses it prevents any inhibition of the heart from stimulation of the vagus or of the junction of the sinus venosus, just as atropin does.

[1] The transient secretion ensuing immediately after injection is not here regarded as a proper effect of a strong dose, since the larger the dose the slighter and more transient it becomes.

ON A NEW STAINING-FLUID. By JULIUS DRESCHFELD, M.D., M.R.C.P., *Lecturer on Pathology, The Owens College, Manchester; Assistant-Physician, Manchester Royal Infirmary.*

FOR the last nine months I have been in the habit of using a new staining-fluid for histological purposes, which I find to have so many advantages over other colouring fluids now in use, that I may be permitted to draw attention to it, since after a very extensive trial I have obtained very satisfactory results from its use.

The fluid in question is a very dilute solution of Eosin, a body which is now manufactured in large quantities, and can easily be obtained from any wholesale chemist.

The mode of application is very simple. The thin sections are put into the eosin solution, which contains about one part of eosin to 1000—1200 parts of water and which presents a sherry-coloured, green fluorescent fluid; they are allowed to remain in that fluid only for one minute to a minute and a-half, are subsequently put for a very short time into water slightly acidulated with acetic acid, and can then be examined either in glycerine or any other of the ordinary menstrua, or can be mounted in Canada-balsam in the usual fashion. If the sections are to be mounted in balsam, it is better to use tissues hardened in alcohol or chromic acid, as with some fresh tissues (but by no means with all), such as cartilage, the eosin when brought into absolute alcohol previous to mounting in balsam is dissolved out.

The action of eosin on tissues is very similar to that of carmine, since it stains chiefly the nuclei and the softer protoplasm; it has, however, several great advantages over carmine, for:

1. The time required for perfect staining does not exceed 1—1½ minutes.

2. The solution is easily prepared, remains perfectly clear, and can be kept without altering or forming a precipitate for any length of time.

3. Eosin has the property of clearing the tissues, and hence even thick sections allow their microscopic structure to be studied with accuracy.

4. In specimens stained with eosin the component parts of the tissue are beautifully differentiated; this makes it particularly applicable in the examination of complicated structures, such as tumours.

The last two properties of eosin are probably due to its fluorescence, for I found the same property in two other highly fluorescent preparations, namely: Fluorescin and Magdala Red. The former of these two bodies clears the tissues without staining them; the Magdala Red stains them purple and is therefore quite as applicable as eosin, but inasmuch as it is very soluble in alcohol, it cannot be used when specimens are to be mounted in balsam.

I have found the eosin staining particularly useful in the examination of nervous tissue. The nuclei and nucleoli of the ganglion cells are stained light pink; the same is the case with the axis-cylinder of the nerve-fibres, and the processes of the ganglion cells, while the medulla of the nerve-fibres is not stained at all; the areolar tissue, on the other hand, receives a much deeper tint than the axis-cylinder.

I find eosin equally useful in examining fresh sections of tumours for diagnostic purposes; and here, I think, it surpasses all other colouring re-agents, owing to the short time of exposure, the clearing up of even thick sections and the differentiation of the component parts, such as the areolar tissue and the cellular elements, so that the histological details come out with very great clearness.

It will be seen from the above that eosin will form a very important and convenient re-agent in the practical courses in histology now universally given; and it has been used with great success in the demonstrations given last session at The Owens College, both in normal histology and in morbid anatomy.

In conclusion, I wish to draw attention to two points in using the eosin solution, namely: to have the solution *very* dilute, and not to allow the specimens to be exposed longer than one minute or one minute and a-half.

NOTES OF A CASE IN WHICH THERE WAS A SMALL APERTURE IN THE SEPTUM VENTRICULORUM NEAR THE APEX OF THE HEART[1]. By DYCE DUCKWORTH, M.D., *St Bartholomew's Hospital* (London).

THIS heart was taken from the body of a male child who was born at full time, and was observed to be 'cyanotic' at the time of birth, and not merely livid from defective respiration.

On examination the several cavities were found to be natural, likewise the auriculo-ventricular and sigmoid valves. Unfortunately the aorta was cut off below the junction of the ductus arteriosus, so that the condition of the latter tube was not ascertained.

In the septum of the ventricles at about the junction of its middle and lower third, and situated somewhat posteriorly, was an opening large enough to admit a crow-quill. The edges were more rounded on the left ventricular aspect. The foramen ovale was pervious and the Eustachian valve well developed.

The lungs were found not to have been expanded, and hence the child cannot have respired.

The history was that the mother was 25 years of age, and had been married four years. She had had two miscarriages, first, a case of twins at the fifth month, secondly, a miscarriage at the seventh month. Her third pregnancy resulted in a healthy child at full time. No history of syphilis was obtained, and the miscarriages appear to have been due to weakness.

No noteworthy event occurred during early pregnancy before the birth of the child whose heart is described. At the seventh month the mother had a fall which was followed by loss of blood.

This case presents the peculiarity of an aperture in the ventricular septum in an unusual situation.

In the great majority of instances where the septum is imperfect, the opening is at the upper part, and just below the respective sigmoid valves[2]. Indeed I am not aware of an example in which this opening has occurred in the lower half of the septum. The imperfection in this case appears to serve no purpose, for, although the ductus arteriosus was not shewn to be pervious, I cannot doubt that it was so, and would have closed at the usual period had the child lived. The condition of the pulmonary artery warrants this supposition.

It seems likely that during systole the small aperture would have been completely closed, and no intermixture of blood-currents would have occurred. Hence the imperfection may perhaps be more strictly regarded as an anatomical peculiarity than as a pathological specimen, and the significance of the pervious septum may be no greater than that of an imperfect foramen ovale.

[1] I am indebted for this specimen to Mr Burgess, obstetric assistant at St Bartholomew's Hospital, in whose practice the case occurred, and who kindly furnished the notes of it.

[2] "On the irregularities of the large blood-vessels." W. Turner, *Brit. and For. Med. Chir. Review*, LIX. 179, 1862.

REPORT ON PHYSIOLOGY. By WILLIAM STIRLING, D.Sc., C.M., M.D. (Edinb.), *Demonstrator of Practical Physiology in the University of Edinburgh*[1].

EULENBURG AND LANDOIS ON THERMAL INFLUENCES PROCEEDING FROM THE HEMISPHERES OF THE CEREBRUM. (Vaso-motor apparatus of the cerebrum.)—Drs Eulenburg and Landois (*Centralblatt*, No. 15, 1876) operated on dogs, and they found that young animals were specially well suited for their purpose. The estimation of the temperature was taken thermo-electrically by means of a Meissner-Meyerstein's electro-galvanometer. As thermo-electrical elements, two varnished Dutrochet needles were employed. After opening the skull and exposing the surface of the brain the grey matter was destroyed by means of red-hot copper wires to the depth of one to one and a half millimètres. The animals were kept deeply under chloroform. When a certain portion of the brain was to be stimulated the animal was curarised, and induction shocks were applied by means of two fine platinum wires which served as electrodes. The chief results were the following:

1. Destruction of certain regions of the anterior lobes of the brain corresponding to the temporal region caused at once a considerable increase of the temperature in both contro-lateral extremities. The increase of temperature occurred immediately after the complete destruction of the corresponding parts of the surface of the brain, often before the animal awoke from the chloroform, and before it made any spontaneous movement. The increase immediately after the operation may be 5° to 7° Cent., in other cases only 1½° to 2° Cent.

2. The thermal areas for the anterior and posterior extremities are separated from each other. The area for the fore-foot lies more anteriorly, and somewhat external, close to the lateral end of the sulcus cruciatus. Destruction of the super-sylvian gyrus has no thermal effects.

3. In successful cases, after the animal awakened from the chloroform, generally there was disturbance of motion, and it seems that the portions of the surface of the brain which have this thermal action must lie in the neighbourhood of the corresponding motor areas.

4. The increase of the temperature is in nearly all cases clearly pronounced for a long time after the injury, sometimes even for three weeks; generally, however, it returns to the normal on the second or third day. Localised electrical stimulation of the above area with sufficiently weak currents is accompanied by a small and

[1] To assist in rendering this report more complete, authors are invited to send copies of their papers to Dr Stirling, Physiological Laboratory, Edinburgh University.

temporary diminution of temperature (0·2° to 0·6° Cent.) in the contro-lateral extremities.

The author is of opinion that these facts justify the conclusion that there is a vaso-motor apparatus in the grey matter of the brain, and that it partly represents the central terminations of the vaso-motor nerves which run in the pedunculus cerebri.

ON THE FUNCTIONS OF THE CEREBRAL HEMISPHERES.—C. Carville and H. Duret (*Archives de Physiol.* 1875, and *Centralblatt*, No. 52).—The first part of this very extended research contains an historical review and criticism of the experiments hitherto made on the function of individual parts of the brain. The authors reject entirely, and with justice too, the results of the experiments of Fournié, obtained by injecting chloride of zinc into the brain of the living animal. Even the results of Nothnagel's experiments they discard (injection of dilute chromic acid). The second part of the paper is devoted to an experimental criticism of the results of Hitzig and Ferrier: the idea of Schiff that the movements caused by stimulation of the surface of the brain are reflex, the authors regard as not supported by fact. They cite experiments performed on living and dead brains, to show that on a certain point of the surface of the brain localised currents extend both laterally and in depth. Two platinum needles connected with a very sensitive galvanometer were placed on the surface of the brain or pushed into it to the depth of several millimètres. On applying weak induction currents to certain parts of the surface of the brain, the galvanometer needle was more or less deflected. Nevertheless, the localised action of the current is to be assumed, inasmuch as stimulation of parts of the surface of the brain discharges different and quite distinct movements when only weak currents are employed, a fact already sufficiently pointed out by Hitzig. With regard to the action of anæsthetics the authors generally agree with Hitzig. A further series of experiments is given to show that the integrity of the grey matter is not necessary for the occurrence of circumscribed movements. Similar experiments were performed by Braun and Putnam. The experiments are new which prove that complete extirpation of the corpus striatum does not hinder the occurrence of movements on stimulation of the surface of the brain, and that distinct bundles of the centrum Vieussenii conduct the excitement from the brain to the periphery. Further, some results of Ferrier are corrected, which were obtained by employing too strong a current. The extirpation experiments do not show anything new. The authors come to the conclusion that the cerebral centres are replaced after their destruction in the grey matter of the same hemisphere.

Further experiments are connected with elucidation of the functions of the corpus striatum and optic thalamus. Concerning the latter the authors confirm the experiments of Ferrier, according to whom electrical stimulation of these structures does not cause either pain or movement. In studying the function of the corpus striatum, one must specially bear in mind the nucleus caudatus and

the corpus lenticulare. Electrical stimulation of the nucleus caudatus yielded the authors the same results as Ferrier, viz., contraction of all the muscles on the opposite half of the body. Complete extirpation caused a great weakening of the opposite half of the body (frequently falling to one side) and a movement in a circle, in which the animal always executed the same movements with the sound feet, and rotated around the affected ones like a top. On injuring the internal capsule, complete paralysis of both extremities of the other side occurs. This occurs upon injuring the anterior portion of the first two-thirds, which lies immediately under the ventricular surface of the nucleus caudatus. Section above the same produces only incomplete hemiplegia. Destruction of the posterior part of the capsula interna (between thalamus opticus and nucleus lenticulare) produces hemi-anæsthesia of the opposite half of the body.

The authors, from their experiments, attempt to locate the probable position of the different centres in the cortex of the brain in man thus:—The centres for the different movements of the upper and lower extremities lie in the middle of both upper posterior cerebral convolutions, in the middle of the anterior cerebral convolutions, and in the whole of the upper temporal lobes.

The centres for the movements of the neck and head lie in the posterior part of the first frontal convolution, where it unites with the anterior central one.

The most probable centre for the muscles of expression and eyelid lies at the place of junction of the second frontal convolution with the anterior cerebral one.

The centre for the movements of the tongue, jaw, and lips are placed in the third frontal convolution (Broca).

Single centres for the movements of the eye-balls are placed, according to Ferrier, in the gyrus angularis. The first temporo-sphenoidal convolution has probably a relation to the organ of hearing. Lastly, the authors give a series of experiments which have a pathological importance. Coma occurs most easily in extensive hæmorrhage into the centrum semi-ovale; perhaps with hæmorrhage on the convexity, and specially of the frontal lobes. If an intra-ventricular hæmorrhage stimulates the ependyma of the ventricle, tetanic convulsions of the extremities on the opposite side of the body result. With hæmorrhage at the base stretching towards the medulla, the phenomena of general tetanus are always to be observed at the moment of the attack.

On the Phenomena produced by Faradisation of the Cortex of the Brain.—Rochefontaine (*Gazette Médicale de Paris*, No. 52, 1875) found when both vagi were left intact, and the superior cervical ganglia of the sympathetic of the dog were removed, that by faradisation of the superior frontal convolution before and behind the sulcus cruciatus, there was an increase of the blood-pressure and the heart-beats. If, however, the superior cervical ganglia were left intact, and the vagi divided between the base of the skull and the nerve-fibres passing from the superior cervical

ganglia to them, then on stimulating the same points on the surface of the brain there was a very considerable diminution of the blood-pressure and of the heart-beats. Stimulation of several parts of the surface of the brain had, therefore, the same effect as stimulation of the depressor nerve. In a similar manner, from four different parts of the surface of the brain, contraction of the spleen was produced; from other points contraction of the intestines. The author concludes from this and from the analogy of the phenomena obtained on stimulation of peripheral sensory nerves, that an unlimited number of sensory points exist on the surface of the brain, whose stimulation acts on the terminations of cerebral centripetal fibres. These conduct the impression to the nuclei of grey matter in the intracranial portion of the cord, from whence it is transferred to centrifugal nerves to produce these various phenomena.

As supporting his view the author cites the experiments of Brown-Séquard (*Journal of Anat. and Phys.* x. 619), who, by the application of the actual cautery to the centres placed in the cortex, did not succeed in causing movements of the extremities.

On the Influence of the Excitation of the Brain on the Beats of the Heart.—Lépine (*Gazette des Hôpitaux*, No. 90, 1875) found that stimulation of the surface of the most anterior part of the cerebrum influenced the heart-beats of the dog. If the *left* vagus was divided in a curarised dog, and the *right* surface of the brain was stimulated, the number of heart-beats was unchanged; if the left side, on the contrary, was stimulated, the number of heart-beats was diminished and the height of the pulse sank.

Physiology of the Cerebellum.—H. Nothnagel (*Centralblatt*, No. 22, 1876), from a series of experiments on the cerebellum of rabbits, has arrived at the following conclusions:—(1) The cerebellum can be stimulated mechanically by a minimum puncture with a needle. (2) The motor phenomena can be discharged from different parts of the hemispheres and from its vermiform process. It is not necessary that the deeper parts adjoining the crura should be stimulated mechanically. (3) Mechanical stimulation of *one* hemisphere of the cerebellum produces motor phenomena first on the one and then on the other side of the body. The same is produced by injury to one side of the vermes; stimulation of the vermes in the middle line produces simultaneously motor phenomena on both sides. (4) One may remove (*a*) the greater part of one hemisphere, (*b*) greater part of both hemispheres, *i.e.* with the exception of the direct continuation of the crura, (*c*) or the entire anterior and upper part of the vermes, and the animal may remain several days without showing any symptoms thereof. (5) Destruction of a distinct portion of the vermes, however, produces intense continued motor disturbances which agree with those described by Flourens.

On the Inhibitory Nerves of the Cutaneous Vessels.—A. Ostroumoff (*Pflüger's Archiv*, Band xii. p. 219) has investigated

the above subject in the laboratory of Professor Heidenhain of Breslau. By the term 'inhibitory nerve' the author means a nerve whose action is to diminish the activity of other nervous apparatus, and this the more, the more energetically it acts. An inverse relation exists between the degree of activity of the inhibitory nerves and that of the inhibited nervous apparatus. The author has sought to determine the condition of the cutaneous vessels by measuring the temperature of the skin. The animal employed was the dog, and the temperature was taken by very sensitive thermometers placed on the interdigital membrane of the foot.

1. *Stimulation of the freshly divided Sciatic Nerve by means of Tetanising Induction Shocks.*—In order to prevent evaporation and drying of the nerve its peripheral end was placed in a T-shaped glass tube, into the vertical stem of which electrodes in connection with the secondary spiral of the induction machine were placed. Stimulation of the peripheral end of the nerve was always followed by a contraction of the vessels, which was not temporary, as indicated by Goltz (*London Medical Record*, Jan. 1876), but lasted for a long time, so that there is not a rapid exhaustion of the nerves producing contraction. The reason of the difference in Goltz's experiments is to be sought in the fact that Goltz stimulated the nerve several days after it had been divided, *i.e.* when degeneration of the nerve-fibres and loss of excitability had already taken place.

2. *Tetanic Stimulation of the Sciatic Nerve three or four days after Section.*—In this case tetanic stimulation was followed by a rapid increase of temperature. The result depends upon the time after section. After six days no result could be obtained.

3. *Stimulation of the freshly divided Sciatic Nerve by means of single Induction Shocks.*—Induction shocks, applied at intervals of five seconds, produced an increase of temperature, which could also be produced, though more rarely, by tetanising with *very weak* currents. From these experiments the author concludes that the sciatic nerve contains the proper vaso-motor fibres, whose stimulation causes contraction of the vessels, together with the inhibitory fibres, whose stimulation is followed by dilatation of the vessels. If the normal nerve-trunk is stimulated with single induction shocks of the proper strength at regular intervals of five seconds duration, the influence of the inhibitory fibres is exerted; if the nerve is tetanised, and the currents do not lie between very limited and very small values, the effect of the vaso-motor fibres is the more pronounced.

After section of the nerve-trunk the excitability of the vaso-motor fibres sinks more rapidly than that of the inhibitory fibres, so that during a certain period after section (three or four days) the excitability of vaso-motor fibres is nearly extinguished. At this time tetanic stimulation, because it acts on the still highly excitable inhibitory nerves, in opposition to the results on the normal nerve, no longer produces contraction, but dilatation of the vessels. The author believes in the existence of peripheral ganglionic apparatus placed in connection with the vessels. The tonus of the vessels

depends upon the great nerve-centres and also upon these peripheral centres, on which two kinds of nerves act—the vaso-motor, by increasing their activity, the inhibitory, by diminishing it. The dilatation of the vessels, following section of the nerve, lasts very much longer than the excitability of the divided nerve itself. The dilatation also in the course of time diminishes, but it never completely disappears. The inhibitory apparatus of the cutaneous vessels is more like that of the salivary glands than that of the heart. The inhibitory nerves of the cutaneous vessels, like those of the chorda tympani, are not affected by a much larger amount of atropine than suffices to paralyse the inhibitory fibres of the vagus, and the secreting fibres of the chorda tympani. The blood-vessels, whose vasomotor nerves are divided, can no longer be regarded as simple elastic tubes, whose diameter is determined alone by the pressure exerted upon the inner surface. Very pronounced increase of the blood-pressure has no obvious dilating effect on the small arteries and capillaries. The pressure within the aorta may be doubled without the temperature of the skin being increased. Such vessels with divided nerves do not, however, conduct themselves exactly like quite normal ones. The capacity of the former to resist fatiguing influences is much more easily exhausted. In the author's experiments the increase of the blood-pressure was produced by stimulating the peripheral end of the great splanchnic. The temperature rose as little in the paralysed as in the normal limb. The activity of the vascular wall therefore must be independent of the nerves passing to it from without. If the sciatic nerve of the paralysed side has been previously stimulated, the increase of the blood-pressure produced by stimulation of the splanchnic has a decided effect upon the temperature. It is therefore proved that: 1st. The blood-vessels, even after division of their nerves, offer great resistance for a long time to the dilating action of the blood-pressure when the latter is suddenly increased. 2nd. That this capacity for resistance is diminished by fatiguing influences. 3rd. That vessels which are still in connection with the central organs are much more capable of developing this resistance, because they are less easily fatigued. It is therefore probable that the peripheral end organs of the vasomotor nerves exercise a regulating influence on the blood-stream.

The inhibitory nerves of the cutaneous vessels may be set in action by (1) reflex stimulation: Heidenhain has already shown that stimulation of the central end of a sensory nerve increases the temperature of the skin; Owsjanikow has shown the same for the inhibitory fibres of the chorda; and Goltz observed that the foot of the other side became normal on stimulating the central end of the sciatic nerve of the other leg in a dog, whose spinal cord had been divided at the last dorsal vertebra. This dilatation of the vessels was here also undoubtedly reflex, as is shown by the author.

Stimulation by suspension of the respiration increases the temperature of the skin (Heidenhain); but blood-vessels whose nerves are divided are not so affected. If, however, the peripheral centra have been exhausted, the increase of pressure produced by sus-

pension of the respiration causes dilatation, but not on vessels with active motor apparatus. The inhibitory nerves may also be excited by nicotine and by physical stimuli.

On the course of the Vaso-motor Nerves from the Central Organs to the Sciatic Nerves.—The author confirms the opinion of Claude Bernard, that the vaso-motor nerves avoid the paths from which the sciatic nerve receives its motor and sensory fibres (sacral plexus) and rise higher up, reaching the sciatic through the sympathetic. Both the vaso-motor and the inhibitory nerves reach the sciatic through the abdominal sympathetic. (1) Section of the sacral roots and their stimulation have both no appreciable direct influence on the temperature of the hind feet. (2) Section of the sympathetic, on the contrary, at the level of the bifurcation of the aorta increases the temperature permanently. (3) Tetanic stimulation diminishes it. (4) Under favourable circumstances rhythmical stimulation causes an increase. (5) Sensory stimulation, injection of nicotine, suspension of the respiration, produce an increase of temperature in the hind foot, even after section of the sacral roots, and this to the same extent as in the normal condition, but no longer after section of the abdominal sympathetic (as low down as possible) even when the sacral roots are intact. The vaso-motor nerves supplied to the sympathetic are derived not only from the lumbar, but also from the dorsal region, though how far up the author has not tested.

Eye.

On the Hydraulic Movements of the Iris, and on the action of some substances on the Pupil.—A Mosso (*Accademia di Medicina di Torino*, 1875) regards as hydraulic movements those movements of the iris which are dependent on filling and emptying the vessels of this structure. The results of his experiments coincide with those of Grünhagen. If a half per cent. solution of common salt, serum, or defibrinated blood is injected under a high pressure through the carotids into the head of a rabbit two days after death, a change in the pupil occurs. The pupil shortly after death can be dilated by the introduction of a solution of atropine, and the condition can be preserved by taking special precautions.

The hydraulic movements depend upon the arrangement of the vessels of the iris. Léber had already shown how the arteries of the iris collectively arise from the large corona iridis, and run in a radial direction towards the margin of the pupil. Most of them bend round in an arched manner to terminate in the origin of the veins. In order to explain the mechanism of the hydraulic movements from the arrangement of the vessels of the iris, Mosso prepared an artificial iris from a thin-walled caoutchouc tube, which was arranged upon a plate of cork. The convolutions of this tube ran here and there between two concentric circles. On the outer circle, which corresponded to the large corona iridis, they were fixed with needles, and at the margin of the pupil they were left

free. With this arrangement it can be shown that filling of the vessel corresponds with a diminution of the pupil, and with every emptying of the tube the artificial pupil dilates. In this way Mosso explains many movements of the iris, which were formerly insufficiently explained by the action of muscles and nerves.

Every dilatation of the vessel produces myosis, whilst its contraction is followed by mydriasis. These results the author can confirm on man by means of his plethysmograph. Mosso had formerly found that every deep inspiration is followed by a contraction of all the vessels. If through a small hole made in a visiting card by means of a needle, one looks at a white wall, the movements of one's own iris may be observed. By this simple method the author observed on himself how every deep inspiration and every contraction of the vessels was connected with a dilatation of the pupil.

The myosis depends sometimes only on paralysis of the vessels, and it is a constant phenomenon in the action of substances such as chloroform, ether, chloral, morphia, etc., which dilate vessels and produce sleep. Conversely, mydriasis occurs every time when, either by poisons or through other conditions, the vessels contract.

Lastly, the author has found that when the pupil has reached the maximum of dilatation by electrical stimulation of the sympathetic in the neck, electrical stimulation of the oculo-motorius within the cranium, or an intense light, can contract the pupil, without, however, producing the minimum of contraction. Conversely, when by action of light the pupil has been almost caused to disappear, it can be slightly dilated by stimulation of the sympathetic, without, however, attaining its maximum.

Von Platen and Pflüger on the Influence of the Eye on the Metamorphosis of Tissue.—O. von Platen and E. Pflüger (*Pflüger's Archiv*, Band xi. p. 272, and *Centralblatt für die Medicinischen Wissenschaften*, No. 8, 1876) are of opinion that that condition of the brain which we term 'waking' is partly at least kept up by a summation of sensory stimuli; that further the waking condition of the brain causes a continual stimulation of almost all the centrifugal nerves, *i. e.* an increase in metamorphosis of tissue. A series of facts may be cited in support of this view—the rapid increase of the temperature of hybernating animals when they have been wakened by strong stimuli; the diminution in the production of carbonic acid during sleep, and also by the action of curara; lastly, the storing up of energy during sleep which cannot be attained so rapidly by simple rest. From this point of view it appears probable, that by removing all stimuli from the retina it ought to be possible to obtain a considerable diminution in the production of carbonic acid. The experiments of Moleschott on this subject, as the authors show, are not sufficient proof, because the greatest insensibility of the retina was not produced; and the same is true of an experiment by Pott.

The experiments of von Platen were made with Röhrig-Zuntz's

respiration apparatus on rabbits, in which tracheotomy had been performed. The rabbits respired pure oxygen, the amount consumed being read off directly. The carbonic acid was absorbed by caustic potash, and after acidulation with sulphuric or phosphoric acid was pumped out and measured. To exclude the light from the retina, rings of wood, in which was placed a piece of glass, were fixed in front of the eye. By means of a lid the light could be excluded. Each period, 'clear or dark,' lasted about twenty or thirty minutes. The periods alternated several times, and commenced sometimes with the one, sometimes with the other. Apart from a few variations, the oxygen absorbed and the carbonic acid given off were greater in the light than in the dark. Of eight animals, in one minute the mean was:—

	In Darkness. Cubic Centimètres.	In Light. Cubic Centimètres.
Oxygen taken in . . .	120·465	140·665 = 100 : 116
Carbonic acid given off .	85·635	97·96 = 100 : 114

Blood and Blood-vascular System.

On some Variations presented by the Total Amount of the Blood.—Malassez (*Archives de Physiologie*, 1875, p. 261, and *Centralblatt für die Medicinischen Wissenschaften*, No. 11, 1876) has continued his researches on this subject in Ranvier's laboratory. By the term 'blood-corpuscle capacity' (*capacité globulaire*), the author expresses the quotient obtained by dividing the absolute number of blood-corpuscles by the weight of the animal expressed in grammes. A rabbit weighing 2,450 grammes has 919,450 millions of blood-corpuscles, and, according to the above, a blood-corpuscle capacity of 373 millions.

By the term 'richness in corpuscle' (*richesse globulaire*), the author means the number of blood-corpuscles contained in a single cubic millimètre of blood. Following these two data throughout the animal series, it is shown that the *capacité globulaire* is greatest in the mammalia (rat 630 millions, rabbit 373 millions). It is generally less in birds than in mammals. It is very considerably diminished in the osseous fishes, more so in the cartilaginous species and the amphibians (torpedo two to six millions, frog seventeen millions, proteus two millions, axolotl one to four millions). The *richesse globulaire* also diminishes in the animal kingdom in the same direction as the *capacité globulaire*, but the two curves do not run parallel, inasmuch as the latter sinks more rapidly than the former. By the small decrease of the *capacité globulaire* the greater diminution of the *richesse globulaire* is counterbalanced, and in a certain sense compensated for.

While in the lower animals both the *capacité* and *richesse globulaire* are less, the dimensions of the blood-corpuscles are much greater. One might assume that the smaller number was thereby compensated. According to the author, this is not so. Under all

circumstances the lower animals are at a disadvantage, and have a smaller quantity of blood than animals higher in the scale.

The author has made extended observations on the influence of age on the number of blood-corpuscles in the rabbit, rat, guinea-pig, dog, cat, chick, and frog larvæ. In mammalia, both *capacité* and *richesse globulaire* rise after birth and reach their highest point in the third or fourth week of life; they then begin to fall, and sink below the point at which they started. In adult animals both seem to rise again considerably. In the chick the *capacité globulaire* scarcely varies during the whole time of incubation; after birth it sinks pronouncedly; it rises again in the adult, without, however, again reaching the height it attained during the embryonal condition.

Investigations on animals under different hygienic conditions, *e. g.* starvation, feeding, etc., gave as the general result that the *capacité globulaire* always diminished when the hygienic conditions were not so good, or when the general condition of the animal was in any way deteriorated. A case of transfusion, in which Malassez ascertained the *capacité* and *richesse globulaire* both of the person who gave the blood, and the one into whom it was transfused, is employed by the author to calculate the quantity of blood in both persons. For the one who received the blood, the quantity of blood was one-seventieth of the body weight; for the other one-ninth, which numbers agree exactly with those of Lehmann, Weber, Welcker, and Bischoff.

On the Blood-current in the Coronary Artery of the Heart.—F. Klug (*Centralblatt für die Medicinischen Wissenschaften*, No. 8, 1876) cites an experiment to prove the truth of a remark of Brücke's, 'That the capillaries during the contraction of the cardiac muscles are so compressed that they are caused to disappear.'

The hearts of two frogs were exposed; the one was ligatured during the systole, the other during the diastole. The hearts were then excised, and placed in dilute sulphuric acid, in order to cause coagulation of the blood. The muscles of the heart stopped during diastole were rich in blood, whilst those of the one ligatured during its systole showed only traces of blood in their outer layers. The same experiment was repeated on a rabbit with the same results.

On the Relation of the Coagulation of Fibrin to the Corpuscles of the Blood.—Alex. Schmidt (*Pflüger's Archiv*, Vol. xi., and *Centralblatt*, No. 11, 1876), in the first part of his communication discusses the cause of the coagulation of the fibrin of the blood. The artificial formation of fibrin from its factors, fibrinogen and fibrinoplastin (and the fibrin ferment, which, as a rule, adheres to the fibrinoplastin), only succeeds when one of the two factors is employed in its natural solution, but the result does not take place when both substances are mixed with each other in a weak solution of caustic soda. This observation forms the basis of the new experiments of the author. In the course of his observations Schmidt

found that the presence of neutral salts is necessary for the formation of fibrin, just as for the coagulation of albumen at a high temperature. If the soluble salts are removed by dialysis from the fluids which, when mixed, yield fibrin, and if the precipitates (fibrin-forming substances) thereby deposited are brought into solution by a minimum addition of caustic soda, and the two fluids be now mixed, no formation of fibrin occurs. If, however, some of the diffusate, concentrated by evaporation, is added, fibrin is excreted. The same effect is produced by adding a solution of common salt to the extent that the fluid contains 0·8 to 1 per cent. For the formation of fibrin, therefore, a certain relative proportion of salts is necessary, and hence the reason why fluids obtained from the body after dilution with water yield less fibrin. Pericardial fluid yielded 0·132 per cent. of fibrin; diluted with an equal volume of water only 0·083 per cent.; plasma of horse's blood yielded 0·726 per cent.; diluted with one-third its volume of water, 0·689; and with an equal bulk of water, 0·617 per cent. If plasma is diluted with ten to twelve volumes of water, only a very inconsiderable excretion of fibrin takes place, and that very slowly. If, on the contrary, Na Cl is added till the fluid contains one per cent. of the salt, the normal amount of fibrin is obtained. Some other salts, as is known, have the same action. Thus, by the addition of one part of a twenty-five per cent. solution of sulphate of magnesia to three or four parts of blood, coagulation may be entirely prevented, while a solution of common salt partly counteracts this effect. By dialysis of fluids which yield fibrin, the active substances are completely excreted in an insoluble form, so that the filtered fluids, on the addition of Na Cl, yield no fibrin, but the part remaining on the filter dissolved in weak caustic soda does.

The author then discusses the question how solutions are to be prepared which contain only one of the three factors necessary for the formation of fibrin.

1. *The Fibrin Ferment.*—The method originally indicated by the author requires correction in one point,—the alcohol must act for a very long time, three or four months, upon the albuminous coagulum. If this is not done, the solution of the ferment also contains fibrinoplastic substance, so that it can cause coagulation in solutions which contain fibrinogen alone.

2. *Fibrinogen.*—Fluids which contain this substance are much more numerous, such as the pericardial fluid of the horse, and hydrocele fluid.

3. *The Fibrinoplastin* is best prepared from egg-albumen, which very rarely contains any trace of ferment. If the salts are removed by rapid dialysis, the fibrinoplastin is excreted in the insoluble form; it is then washed in water and employed either solid or in solution.

After having prepared these three substances, one may convince himself of the necessity of all three for the production of coagulation. Coagulation occurs with a neutral, feebly alkaline, and feebly acid reaction; a distinct acid reaction prevents it entirely. The quantity of fibrin obtained depends on the temperature. The physical condition of the fibrin depends upon the rapidity of its excretion. If this

occurs very slowly, the coagulum is very loose, breaks up easily, and is generally re-dissolved in the course of twenty-four hours, so that it entirely disappears from view. In another section the author treats of the dependence of the quantity of fibrin on the quantity of the fibrinoplastic substance added. To equal quantities of transudations or blood-plasma—when necessary previously deprived by filtration at 0° of colourless corpuscles—varying quantities of pure precipitated fibrinoplastin, either in the solid form or dissolved in soda, were added, and the fibrin formed was, after twenty-four hours, separated by filtration, washed with water, alcohol, and ether, dried and weighed. In the later experiments, in order to hasten coagulation, a small quantity of dissolved amorphous hæmoglobin was added. It is shown that up to a certain limit the quantity of fibrin increases with the amount of fibrinoplastin added, but not in direct proportion thereto. If too much fibrinoplastin is added, coagulation is very imperfect. Experiment II., hydrocele fluid free from fibrinoplastin, may serve as an example:

	Fibrinoplastin added (f.)	Fibrin obtained (F.)	F. f.
1.	0·462	0·087	0·19
2.	0·924	0·098	0·11
3.	1·386	0·106	0·08
4.	1·848	0·116	0·06

The addition of hæmoglobin accelerates the excretion of fibrin, but does not increase the amount excreted. Solutions of fibrin ferment injected into the jugular vein of the living animal do not produce coagulation, notwithstanding that the blood at first contained a considerable amount of the fibrin ferment, which had not entirely disappeared after twenty-four hours. It is therefore shown that the living organism gradually destroys the fibrin ferment, and paralyses its action in some way as long as it exists. The author then replies to Eichwald, Gorup-Besanez, and Heynsius, for which we must refer to the original.

On the Relation of the Coagulation of Fibrin to the Colourless Elements of the Blood.—A paper on this subject, by Alexander Schmidt, is contained in *Pflüger's Archiv*, Vol. xi. p. 515, and *Centralblatt*, No. 25, 1876.

I. *On the Origin of the Fibrin Ferment.*—It can be easily shown that the coloured corpuscles have nothing whatever to do with the fibrin ferment. 1. There are fluids which though containing no coloured corpuscles coagulate after removal from the body: from the serum, by precipitation by alcohol, a solution of the ferment may be prepared. 2. Plasma of horse's blood poured off from the red blood-corpuscles which had been allowed to subside contained at the moment of their separation from the blood-corpuscles only traces of the ferment. Nevertheless it coagulated at the ordinary temperature and produced serum containing a ferment. 3. If for the preparation of the fibrin ferment, defibrinated horse's blood is employed in which the cor-

puscles have been allowed to subside, solutions of less potency are obtained from the lower layers consisting almost entirely of blood-corpuscles than from the upper. In non-defibrinated blood from the lower layers consisting of blood-corpuscles no active solution of the ferment can be obtained. The source of the fibrin ferment is the colourless blood-corpuscles; it arises from these after removal of the blood from the body, and then passes into the fluid. The proof of this is shown by filtration of the plasma. If the blood of a horse is caught in a glass vessel, placed in ice, and the blood-corpuscles allowed to subside, then when the temperature has fallen to 0° C., and the plasma filtered through several sheets of filtering paper into a vessel at 0° C., a perfectly clear, generally somewhat red-coloured filtrate quite free from blood-corpuscles, and only showing the slightest tendency to the formation of fibrin, is obtained. If a portion of filtered and of non-filtered plasma are exposed at the ordinary temperature of the room, the former coagulates much later than the latter and the coagulation does not end for a very long time. Complete absence of coagulation is therefore not to be expected, because the blood-corpuscles begin to form the ferment at once after their removal from the body, and this process cannot be instantaneously prevented by cooling. When the filtered fluid is allowed to stand, the amount of the fibrin remains unchanged, whilst that of the non-filtered fluid continually increases. This difference between filtered and non-filtered plasma can be tolerably completely prevented if the plasma is warmed to 10° or 20° for several minutes before filtration, and then cooled. The residue extracted with water is dissolved in weak alkaline fluid, and consists of a weak opalescent solution of fibrino-plastic substance containing only traces of ferment. Corresponding to these observations, transudations which appear to be turbid through the presence of colourless elements regularly coagulate; whilst perfectly clear transudations show no tendency to spontaneous coagulation, which, however, occurs on the addition of the ferment. The dependence of coagulation on the colourless corpuscles can also be shown by adding various quantities of suspended colourless corpuscles to the plasma; that portion to which the largest number of corpuscles has been added coagulates much more rapidly than the others. If two portions of the same plasma are taken, and one of these is left to itself, whilst the blood-corpuscles in the other are regularly distributed by repeated stirring, then the subsided layer coagulates first in the first quantity, then the second quantity, and lastly, though much later, the fluid standing above the coagulum. This experiment shows that the impulse to coagulation does in fact proceed from the lymph-corpuscles. The action of non-crystallised hæmoglobin in accelerating coagulation occurs more pronouncedly the smaller the amount of ferment in solution, and the slower it coagulates without the addition of hæmoglobin. Solutions of crystallised hæmoglobin do not produce any accelerating effect.

II. *On the Origin of Fibrinoplastic Substance.*—If plasma is filtered and the residue extracted with water and then treated with

slightly alkaline water, a filtrate is obtained which contains a considerable amount of fibrinoplastic substance in solution. The residue on the filter consists only of colourless blood-corpuscles, from which by solution fibrinoplastic substance has exuded. The objection that the filter residue contains fibrinoplastic substance, which has no connection with the colourless corpuscles, and is excreted in consequence of the cooling, is refuted by the fact that filtered plasma is able to dissolve fibrinoplastic substances added to it. Fine granules are excreted from the plasma. These do not consist of fibrinoplastic substance, but are the remains of disintegrated colourless corpuscles which are constantly mixed with the fibrin, and at the first are easily recognised as such, but in the later stages of coagulation disappear more and more. The decomposition products of the colourless corpuscles increase the weight of the fibrin. This fact can be proved by estimating the amount of fibrin in the filtered plasma. A filtrate completely free from fibrinoplastic substance is never obtained, because the disintegration of blood-corpuscles can never be entirely avoided. Nevertheless the author obtained from filtered plasma only 0·35—0·45 per cent. against 0·5—0·7 from the non-filtered:—the amount of fibrin obtained from the filtered plasma when a solution of fibrinoplastic substance is prepared from the colourless elements and added to the filtered plasma. The difference in the quantity of the fibrin produced becomes much greater when the plasma before filtration is treated with twelve to fifteen times its volume of water. In this case also by the addition of fibrinoplastic substance the amount of fibrin is again increased. Plasma diluted with ten to fifteen times its volume of water remains fluid for an unlimited time at 0° C. The colourless corpuscles sink rapidly, so that the supernatant fluid can be poured off after twenty-four hours, and the blood-corpuscles can be purified by washing with cold water. If after washing they are mixed with a solution of fibrinogen, or better, if fibrinoplastic substance precipitated by carbonic acid or acetic acid and suspended in water is added to the fibrinogen fluid, there results an exceedingly slow coagulation, because only traces of ferment are present.

We have now to ask whether the colourless corpuscles also contain fibrinogen. This question is to be answered in the negative for mammalian blood; for if the washed corpuscles are dissolved in weak alkali and fibrin ferment be added, coagulation never occurs. On the contrary, the solution obtained from the corpuscles of the blood of birds and of amphibians always exhibits a spontaneous coagulation. The fibrin of the blood of amphibians is characterised by its greater solubility in alkalies and acetic acid, but becomes, however, less soluble by washing with water. Frogs' blood coagulates very rapidly, but again becomes fluid in the course of forty-six hours by the fibrin dissolving in the alkaline serum. If the blood-corpuscles are allowed to subside in the defibrinated blood, and the serum poured off, by the addition of water and the solution of the blood-corpuscles, a new coagulum forms, which again becomes dissolved in several hours. The blood-corpuscles, therefore, of the frog undoubtedly contain fibrinogen; and also those of the bird. Whether this proceeds from

the colourless or the coloured corpuscles is doubtful. The assumption that similar conditions are true for the coloured corpuscles of mammalian blood can at present be neither refuted nor proved.

Lymph.

ON THE INFLUENCE OF CURARA ON THE QUANTITY OF LYMPH, AND THE EMIGRATION OF THE COLOURLESS CORPUSCLES OF THE BLOOD.—J. Tarchanoff (*Archives de Physiologie*, November, 1875, p. 33) combats the assertion of Drozdoff that curara dissolves the colourless corpuscles of frogs. Of four sorts of curara which Tarchanoff added in a concentrated solution to the colourless corpuscles suspended in frog's serum, two produced after a long time a solution of the colourless corpuscles; several, however, showed that the free granules remained completely undissolved. Whether this phenomenon depends upon accidental impurities in the curara, the author leaves undecided; the two other portions of the poison were completely inactive. If curara was injected subcutaneously into a frog, a pretty large dose being given, but not sufficient to paralyse the heart, the number of colourless corpuscles diminished and that of the coloured increased; the number of the former (from a series of experiments conducted after the method of Malassez) contained in a cubic centimètre of blood fell to about half of the normal; the latter rose to double. After the return of mobility, *i.e.* after four or five days, the normal condition returned. As the cause of this condition of the blood is to be regarded a very great increase of lymph, very rich in colourless corpuscles, and which coagulated very rapidly, not only in the dorsal lymph sac, but also in other lymph sacs of the body. Specially well filled was the sac underneath the tongue. [This pronounced filling of the lymph sac was known to Bidder, who referred it to paralysis of the lymph-hearts.]

The author, in confirmation of several papers emanating from Ludwig's laboratory, assumes an increased transudation from the blood-vessels of curarised animals. A lively emigration of colourless elements was directly observed in the tongue and mesentery of curarised frogs. This also occurred when the cerebro-spinal axis was carefully destroyed without hæmorrhage. In both cases the author assumes as the cause of emigration an increased transudation and increased lateral pressure in the small arteries in consequence of the extinction of the tonus. As long as the paralysis continued the blood became poorer in serum and white elements. With cessation of the paralysis the pronounced diminution stopped; the lymph sac emptied itself again, and the normal condition of affairs was soon restored. This emptying could also be produced by electrical stimulation during the period of paralysis.

In conclusion, the author makes some objections to Cohnheim's doctrine of suppuration. The condition of curarised frogs proves that enormous outwandering of colourless corpuscles can take place, and is not to be identified with suppuration. In addition, the author has convinced himself, like Malassez, that with continued suppuration,

the number of white blood-corpuscles does not diminish, but rather increases. Further, Ranvier has lately observed the direct division of white blood-corpuscles.

Lastly, the author cites some results upon the distribution of curara in the tissue juices and upon its excretion. For testing its presence he employed the physiological method. The blood of large strong curarised frogs never showed, when it was injected into the lymph sac of small frogs, poisonous properties. Only in very small animals it produced a slight muscular weakness which rapidly disappeared. The bile and lymph gave negative results; the urine on the contrary was very poisonous, and this took place from the beginning of the curarisation, and during the entire duration of the paralysis. If the cloaca was occluded, the urine stagnating in the bladder lost its poisonous properties. Under these circumstances, therefore, the curara is destroyed.

Respiration.

On the Relation of the Excretion of Carbonic Acid to Change in the Bodily Temperature.—H. Erler (*Dissertation*, Königsberg, 1875, and *Centralblatt*, No. 13, 1876) employed for the above purpose rabbits, a caoutchouc cap being firmly fixed over the nose. The respiration was kept up through a Müller's valve, and the expired air passed through a Geissler's potash apparatus. The increase in weight of this apparatus at the end of the experiment represented the amount of carbonic acid excreted. In front of this apparatus there was placed a vessel with a solution of caustic baryta, in order to absorb any carbonic acid which might not have been taken up by the potash. In some cases, where the difficulty of respiration appeared too great, the apparatus was connected with an aspirator.

1. *Carbonic Acid given off when the Animal was tied down.*—In every animal the amount of carbonic acid given off in the free condition was estimated for several periods of ten minutes each, then the animal was tied down, and the amount again estimated several times at the same intervals. The following table gives the mean for the carbonic acid given off:

	Carbonic Acid in ten minutes.	
	Free.	Tied down.
No. 1. .	0·050 grammes.	0·042 grammes.
„ 2. .	0·074 „	0·059 „
„ 3. .	0·045 „	0·029 „
„ 4. .	0·050 „	0·031 „
„ 5. .	0·045 „	0·022 „

The weight of the rabbits varied between 1·020 and 1·372 grammes. The variations in the values are pretty considerable, but in every case the carbonic acid given off diminishes when the animal is tied down, and simultaneously there is a fall in the temperature.

2. *Carbonic Acid given off in the Paralysed Condition.*—This was produced by dividing the spinal cord. The temperature did not rise after this operation, but fell without exception, and that continually, as has been observed several times before. In three experiments the mean values were the following:

	Carbonic Acid in ten minutes.	
	Normal.	Paralysed.
No. 1. .	0·046 grammes.	0·008 grammes.
„ 2. .	0·074 „	0·017 „
„ 3. .	0·091 „	0·016 „

3. *Carbonic Acid given off during Artificial Cooling.*—For this purpose the animals were placed in a double-walled zinc box filled with ice. The body-temperatures obtained by this means are indicated in the following tables:

	Lowest Temperature of body.	Carbonic Acid in ten min.	
		Normal.	Cooled.
No. 1. .	32·34° Cent. (90·32 Fahr.)	0·049 gr.	0·024 gr.
„ 2. .	32·7° „ (90·86 „)	0·039 „	0·014 „
„ 3. .	33·6° „ (92·48 „)	0·034 „	0·016 „
„ 4. .	34·4° „ (93·92 „)	0·061 „	0·028 „
„ 5. .	33·2° „ (91·76 „)	0·039 „	0·016 „

4. *Increased Body-Temperature.*—The box employed for these experiments, instead of being filled with ice, was filled with warm water. The quantity of carbonic acid given off increased when the temperature of the body began to rise, but sank again as soon as the animals became dyspnœic, which generally occurred at 39·4° C. (102·92° Fahr.). If the temperature of the surroundings is very high, then the dyspnœa occurs so soon that no increase of the carbonic acid is to be observed. As the animals for this experiment must be tied down the carbonic acid at the beginning of the experiment diminishes somewhat compared with the normal.

5. *Carbonic Acid given off by diminution of the Bodily Temperature, the Skin being covered with Varnish.*—Here also the excretion of carbonic acid fell, and simultaneously the temperature. The mean value of carbonic acid excreted in all the experiments was in the normal state 0·033, varnished 0·013 grammes. The temperature was reduced to 32·3° C. (90·14° Fahr.). Thus the amount of carbonic acid excreted and the temperature of the body stand in direct dependence one on the other.

Absorption.

ON ABSORPTION FROM THE HUMAN DIAPHRAGM UNDER DIFFERENT CONDITIONS.—A. Rajewsky (*Virchow's Archiv*, Vol. LXIV. p. 186)

removed carefully the human diaphragm and stretched it, avoiding tension, over a funnel, or laid it on a plate and covered its abdominal surface with a thin layer of a solution of china ink in salt solution or with milk. The following results were obtained:—1. The human diaphragm has the property of sucking up fluids which contain suspended particles, just as is the case with the diaphragm of the rabbit, as was shown by von Recklinghausen. 2. The human diaphragm, when it has been changed by inflammatory processes, acquires the property of permitting fluids brought in contact with it to pass into its channels. 3. In diaphragms which have undergone inflammation, by the smallest pressure there may be obtained an injection of the 'saftcanälchen system.' This system is connected with the lymphatic capillaries, and does not consist of mere spaces or slits, but of special canals, which are formed in the loose connective tissue. 4. Removal of the epithelial lining of the serous membrane, either naturally (by inflammation) or artificially, opens new channels for the passage of the fluids, viz. the 'saftcanälchen,' which begin on the free surface of the serosa. 5. From the serosa only small lymphatic stems can be followed into the subserous adipose tissue, where they become united into a network of the finest lymphatic capillaries, in each of whose meshes is placed a fat-cell. The experiments were made in the laboratory of Professor von Recklinghausen, of Strasburg.

Digestive System.

GRÜTZNER ON THE FORMATION AND EXCRETION OF PEPSIN.—P. Grützner describes some new investigations on the formation and excretion of pepsin (Breslau, 1875, 8vo, pp. 86, and *Centralblatt für die Medicin. Wissenschaften*, No. 52, 1875).

I. *On the estimation of pepsin.*—The author gives more exact details regarding his colori-metric method. He recommends the filling of a series of equally thick test-glasses with solutions of carmine of different strength for comparison. Carmine is dissolved in ammonia and diluted with glycerine until a 0·1 per cent. solution of carmine is obtained. Of this solution of carmine, 0·1 cubic centimètre is dissolved in 19·9 cubic centimètres of water, 0·2 in 19·8, etc., up to 1·0 cubic centimètre in 19 cubic centimètres of water. One can, of course, only regard the colour of the fluid by solution of the coloured fibrin as a measure for the quantity of pepsin, as long as some fibrin remains uncoloured. The differences of several fluids containing unequal quantities of pepsin become indistinct when the action lasts for a very long time, as the weak solution of pepsin ultimately dissolves all the fibrin. Then there follows a critical and experimental treatment of the question whether pepsin is used up during digestion. The experiments of the author were made thus. Relatively large quantities of HCl and pepsin were treated with different quantities of fibrin. Large quantities of fibrin constantly required longer time for their solution than when the amount was small; at least, this is true of not too concentrat-

solutions of pepsin. In other experiments, the solutions of pepsin were allowed to act for varying periods of time on fibrin, and then the amount of the pepsin in the fluid was estimated by the colorimetric method. In such cases the amount of pepsin was smaller the longer the action of the fibrin on the fluid had lasted. It therefore follows that *pepsin is used up during digestion.*

II. *The quantity of pepsin in the stomach under different physiological conditions.*—Schiff asserted that certain substances, *e.g.* dextrine, on being introduced into the stomach, or by direct introduction into the blood, were able to increase extraordinarily the quantity of pepsin in the mucous membrane of the stomach, to load the gastric follicles with pepsin. These results had never been confirmed. The author ascribes the error in Schiff's results to this:—that Schiff by his method of extracting the mucous membrane with small quantities of slightly acidulated water obtained very varying quantities of pepsin in solution. The quantity of pepsin obtained under these conditions does not bear any relation to the quantity of pepsin actually contained in the mucosa; mucous membranes poor in pepsin appear to give up their pepsin easily. In addition, many substances when introduced into the blood possess the property of changing the mucous membrane of the stomach so that it gives up its pepsin more easily. The author shows that common salt possesses this property, and so does one of Schiff's peptogenic substances—viz. dextrine. By employing the method of Schiff one obtains results similar to his; still the conclusions he drew from his experiments were erroneous.

On the quantity of pepsin under different physiological conditions.—The mucous membrane with the muscular coat removed was washed and dried on blotting paper. On drying, the submucous tissue for the most part adheres to the paper; the dried fragments were powdered and preserved in an exsiccator. This preparation was extracted with glycerine and then with 0·1 per cent. of hydrochloric acid. The glycerine extract represents the free pepsin, the acid one the fixed. For 0·1 gramme of the dried mucous membrane, 8 cubic centimètres of glycerine, and the same amount of hydrochloric acid, were employed; extraction with glycerine lasted eight days, that with hydrochloric acid twenty hours. Of the extracts so obtained 0·1 cubic centimètre, or, when the pylorus had been used, 0·5 cubic centimètre was treated with 15 cubic centimètres of hydrochloric acid of 0·1 per cent. and fibrin. The microscopic investigation of the mucous membrane was conducted after hardening in alcohol, the sections being coloured with carmine, picro-carmine, or aniline blue. Stomachs of the dog, cat, pig, and rabbit were employed. The results obtained were the following:—(1) The quantity of pepsin in the mucous membrane varies. (2) It varies with different conditions of the peptic cells; if these be bright and large, they contain much pepsin; if they be shrivelled and turbid, little; a moderate size and turbidity correspond to a medium amount of

pepsin. (3) What is true of the peptic cells of the fundus is also true of the same cells of the pylorus; large clear cells indicate a large amount of pepsin. (4) The turbidity of the peptic cells is a sign for the secretion of pepsin. With regard to the relation of the formation of pepsin to the food taken, the following are the results in the dog, the pylorus being employed. The quantity of pepsin increases from the time of taking food till about the ninth hour thereafter; it falls slowly till the thirteenth, and again rises slowly till the fortieth, and then remains so. The fundus, after the introduction of food after long fasting, yields very rapidly a great quantity of pepsin till about the ninth hour. At this time the minimum quantity in the fundus corresponds with the maximum quantity in the pylorus. From this point onwards the quantity rises till the thirtieth hour after food, and remains so for fifteen to twenty hours. If the fasting lasts longer (sixty or seventy hours), a spontaneous secretion occurs, the quantity of pepsin in the fundus diminishes. The conditions are similar in the cat, only here the first period lasts eighteen instead of nine hours. Similar results occur in the pig; in the rabbit, on account of the stomach always remaining full, the stages of secretion are not so clearly pronounced.

III. *The secretion of pepsin observed in dogs with gastric fistula.*—In the fasting condition scarcely any secretion takes place in the stomach. A fluid of alkaline reaction is generally discharged from the fistula—viz., the saliva which has been swallowed; only exceptionally does this contain pepsin. If indigestible substances which powerfully stimulate the stomach are introduced into it, a profuse secretion of a very active gastric juice takes place, which soon (at most one or two hours) becomes much less active; six or seven hours after the introduction the quantity of pepsin again rises. Similar results occur on introducing foods. The increase in the quantity of pepsin from the sixth to the seventh hour is due to activity of the parts near the pylorus. The conditions for secretion are altered, however, when foods are introduced into a stomach not quite empty, as under ordinary circumstances is generally the case. The quantities of pepsin secreted by a stomach twelve to fourteen hours after a good diet on the introduction of more food are much smaller than after a continued long fast. The quantity of pepsin in the gastric juice diminishes continually; an increase in its quantity is not to be observed at any time. In the case of a dog suffering from an intense catarrh of the stomach for several weeks, produced by introducing some pebbles into it, the secretion was continuous, and was not, or but slightly, affected by the taking of food. The juice secreted was turbid, sticky, not always of acid reaction, sometimes neutral and even alkaline; it always contained pepsin, but sometimes extremely little. The author therefore recommends in cases of chronic catarrh of the stomach that only small quantities of food should be given at once, and soon thereafter 30 to 40 cubic centimètres of a 0·04 per cent. solution of hydrochloric acid.

IV. *On the participation of chlorides in the secretion of pepsin.*—If a pylorus which has been washed is extracted with glycerine, one generally obtains a very weak extract. If the pylorus is treated with solution of common salt the extract is very much more active. The common salt breaks up a compound in which the pepsin in the pylorus is contained. If the common salt has also this action in the organism, mucous membranes rich in pepsin must also be rich in common salt. In fact, a series of experiments showed that the quantity of common salt in the dried mucous membrane varied from 0·6 to 1·5 per cent., and the large amount coincided with enlarged and clear peptic cells which contained a large quantity of pepsin. If a large quantity (10 grammes) of common salt be injected into the veins of a fasting dog, the pepsin is excreted more rapidly, so that one hour after the beginning of the experiment the mucous membrane is always thinner than in the animal used for the control experiment. This observation agrees with that of Braun on the increase of the secretion after chloride of sodium.

Liver.

ON THE SECRETION OF THE LIVER.—N. Socoloff (*Pflüger's Archiv*, Vol. XI. p. 166) has tested the assertion of Huppert and Schiff that glycocholic acid injected directly into the blood or absorbed from the intestine is for the most part again excreted by the liver. The author's experiments were made on a large dog with a biliary fistula. Solutions of glycocholate of soda were injected into the jugular vein (0·4 gramme and 0·8 gramme) and into the stomach (1 to 2 grammes). Before and after the injection the quantity of glycocholate acid in the bile, collected at intervals of half an hour, was estimated. Although in individual cases the quantity of bile was increased, an increase of the bile acids was not observed, and no glycocholic acid was detected in the bile excreted. The author therefore rejects the view of Huppert and Schiff. The increase of the secretion cannot be ascribed to the introduction of the water, but is rather to be regarded as the result of a specific stimulating action of the salts of the bile-acids.

Spleen.

ON THE CONTRACTION OF THE SPLEEN AND ITS RELATION TO THE LIVER DURING STIMULATION OF THE SPLENIC NERVES.—Drs Drosdoff and Botschetschkaroff (*Centralblatt für die Medicinischen Wissenschaften*, No. 5, 1876) were led by the observation of Botkin that the liver increased in size where the spleen contracted under the influence of the induced current, to investigate the relation of the spleen to the liver.. The spleen and liver were exposed in a narcotised dog. The quantity of blood in the portal system was estimated by introducing a manometer into the splenic vein; the results were the following. 1. On section of the nerves of the splenic plexus

the spleen increased in all directions, and on stimulating the peripheral ends of the nerves it diminished in size. 2. When the contraction of the spleen produced by stimulating the peripheral ends of the nerves commenced, the liver began to increase in size. The hepatic lobules became sharply defined, their colour deepened, and their tissue became firmer. When the spleen increased the liver again became smaller, its borders sharper, the outlines of its lobules disappeared, its tissues softened. 3. After every contraction of the spleen the number of white blood-corpuscles in the liver increased. This observation agrees with the results of Tarchanoff and Swän (*London Medical Record*, Aug. 1875). 4. Stimulation of the splenic nerves increases the pressure in the vena lienalis. Ligature of all the splenic vessels does not completely extinguish the power of the spleen to increase and to contract, but only diminishes this property.

Kidney.

ON THE PHYSIOLOGY OF THE KIDNEY.—Von Wittich (*Arch. für Mikros. Anat.* Vol. XI., and *Centralblatt für die Medicinischen Wissenschaften*, No. 3, 1876) remarks, that if five cubic centimètres of a solution of ammoniacal carmine are injected into the jugular vein of a rabbit, death ensues in about fifteen minutes. If an examination is then made, not only the ureters, but generally the bladder also, are found to be filled with a red secretion. The microscopic examination of the preparation hardened in acidulated alcohol revealed the following appearances. The surface of the glomeruli was generally of a diffuse red colour, with irregular granular particles lying on them. There is no appearance of a more intense coloration of the nuclei of the vessels of the glomerulus, or of the layer of cells covering them. Between the glomeruli and the capsule there exists a colourless space. The epithelium of the capsule is not tinged. The lumina of the convoluted tubules are filled almost throughout their entire length with masses of carmine, whilst the cells lining the tubules are always colourless. The straight tubules are generally filled with carmine. From these observations it appears (as was shown by Chrzonszczewsky) that the excretion of the carmine begins pretty regularly in the capsules of the glomeruli and that then the excreted particles pass along the tubuli contorti into the tubuli recti, without the gland-cells however being implicated in the process.

The author shows that in from forty to fifty seconds after the injection of the carmine into the jugular vein the first portion of the urine tinged with carmine passes from the pelvis of kidney into the ureter. In the rabbit seven days elapse before the last traces of the five decigrammes of carmine injected are excreted by the kidneys. The same experiments performed on pigeons showed, without exception, accumulation of the carmine in the lumen of the tubules, whilst the accumulation of the urinary constituents proper, *i. e.* of the urates, takes place in the cells of the tubules.

There is therefore a remarkable difference in the relation of the kidneys to an ammoniacal solution of carmine and to sulphindigotate of soda, the latter, as was first shown by Heidenhain (*London Medical Record*, I. 823), and confirmed by Von Wittich, being excreted by the cells of the convoluted tubules. Injection of these two substances simultaneously showed these differences most pronouncedly, although the author is unable to assign a reason for these appearances; nor did the introduction of these substances by the lungs serve to explain the result. Exactly the same results were obtained with the ammoniacal carmine as when it was injected into the blood directly; whilst the introduction of the indigo-carmine by the trachea was disadvantageous, inasmuch as this colouring matter could only be found in traces in the cells of the tubules.

In conclusion, the author remarks that because the cells of the tubuli contorti remain uncoloured during the excretion of carmine we are not entitled to conclude that they do not take a part in the process. From the investigations of Gerlach we know that carmine does not adhere to living cells; it is therefore not impossible that the carmine, like the indigo-carmine, may have passed through the cells of the tubuli contorti, without however being fixed by them. But the opposite peculiarity must be shown in the case of indigo-carmine, viz., that it can be precipitated in the protoplasm of living cells.

Muscle.

ON RED AND PALE TRANSVERSELY STRIPED MUSCLES.—E. Meyer (*Reichert and Du Bois Reymond's Archiv*, 1875, p. 217) found that the primitive bundles of the red semitendinosus were distinctly thicker than the fibres of the pale adductor. While ten fibres of the semitendinosus, from a longitudinal section, lay in the field of the microscope, it required sixteen to twenty of those of the adductor to fill the same space. The nuclei of the fibres of the red semitendinosus were much more numerous and broader than those of the adductor. In the former five nuclei appear on transverse sections, in the adductor only two. The capillaries of the semitendinosus are also characterised by having little aneurysmal dilations. It is shown that all the red muscles of the rabbit have not the same structure as the semitendinosus. Thus it is proved that the cause of the difference of the semitendinosus and adductor is different from that which occasions the difference between the red and pale muscles of the rabbit. There must be a special relation between the semitendinosus and the adductor, which does not exist between the latter and the other red muscles. This relation can only consist in factors, which are present not only in the rabbit, but belong to the whole tribe of the rodents. The difference between the semitendinosus and adductor is not a special peculiarity of all rodents; it is only found in the guinea-pig. Inasmuch as the rabbit and guinea-pig, in opposition to the other rodents, have this in common, viz. that they have been domesticated, so the

author believes that the cause of the partial change of colour in the muscle is to be ascribed to the imperfect movement of the parts in consequence of the domestication. From this point of view it must be shown that other animals, which have undergone a similar process of breeding, show differences in colour. In fact, similar conditions (as far as the difference between the red and pale muscles is concerned) exist in the common fowl. Electrical stimulation showed that the semitendinosus of the rabbit passes into tetanus when pronounced twitching is still clearly visible in the adductor. The semitendinosus seems to be used in a way differing from that of the other muscles of the rabbit; and the author believes that this muscle, in consequence of its being in constant use and in a state of tension in the living rabbit, has lost the power of passing rapidly from one condition into another. Thus the differences between the pale and red muscles have first been acquired partly on account of their different uses, and have been produced in different domestic animals in consequence of domestication and imperfect movement.

Miscellanea.

On the Toxicology of Caffein.—Binz observed some time ago that the temperature of the body was considerably increased after large doses of caffein. J. Perretti (*Dissertation*, Bonn, 1875, and *Centralblatt für die Medicinischen Wissenschaften*, No. 52, 1875) has made numerous experiments on dogs, cats, and rabbits, and found that there was an increase of temperature of 1·4° Cent. (2·51° Fahr.) after the subcutaneous injection of half a gramme of caffein into a dog weighing 2,700 grammes (about 6 lbs.). The effect does not last long, like all the other phenomena produced by the drug. During the increase the animal is in a state of general muscular tension, and it appears to the author highly probable that a direct excitation of the spinal cord and the increased innervation of the motor apparatus dependent thereon cause the great production of heat. The pulse is simultaneously much increased, the salivary glands secrete profusely, and the sensorium is obviously excited. The respiration is rapid, and is paralysed by fatal doses. That artificial respiration can avert death (Uspensky) is confirmed. Neither rigor mortis nor increase of temperature occur, even when the dose is so large that paralysis of the respiratory centre takes place. The spasms from poisoning with caffein do not, as a rule, appear in animals when artificial respiration is kept up, nor in curarised frogs, nor in the extremities after division of the nerves, at least not in frogs. In poisoning with caffein alcohol seems to be valuable. Three experiments show that quite another picture is presented when caffein and alcohol are given simultaneously. The temperature of the intoxicated animal rises again; the affection of the brain becomes less, and the inability for movement passes into violent effort to move. If the dose of the antidote is too strong, then it unites its effects with that of the alcohol.

TRANSMISSION OF ARTIFICIAL ALTERATIONS TO TWO GENERATIONS.—E. Dupuy (*Gaz. Med.*, No. 33, 1875) showed the Society of Biology of Paris guinea-pigs, which presented the peculiar changes in the medulla following section of the cervical sympathetic. These guinea-pigs were the offspring of animals which had inherited this peculiarity from their parents originally operated on. Here, therefore, there was a transmission of an artificially produced condition to the second generation.

Fig. 1.

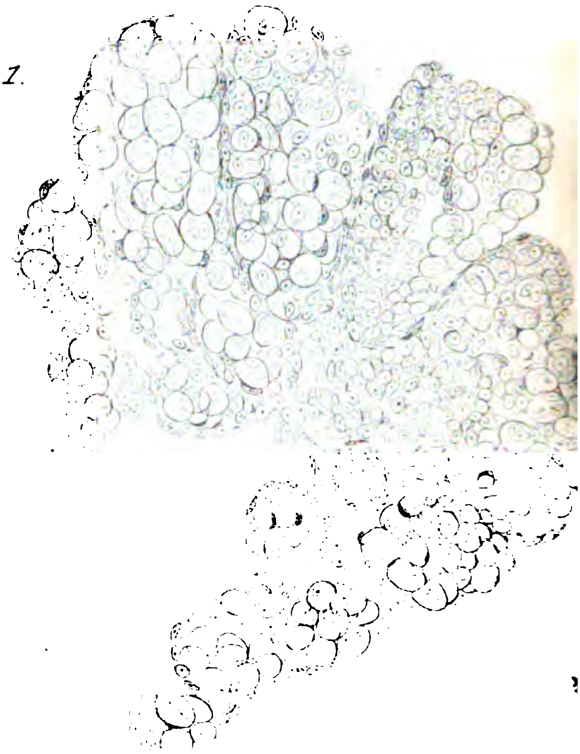
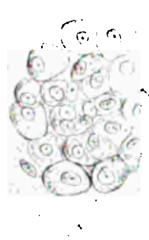


Fig. 3.

a

b



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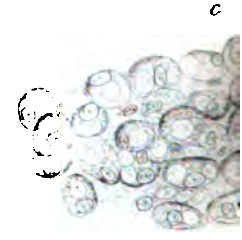
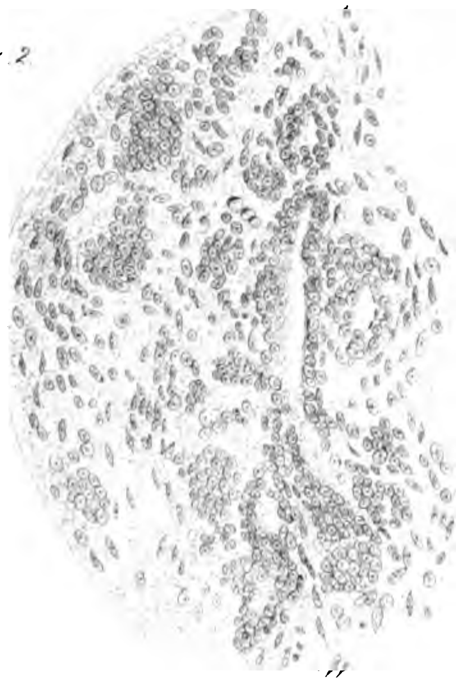


C. Creighton delt

Fig. 2.



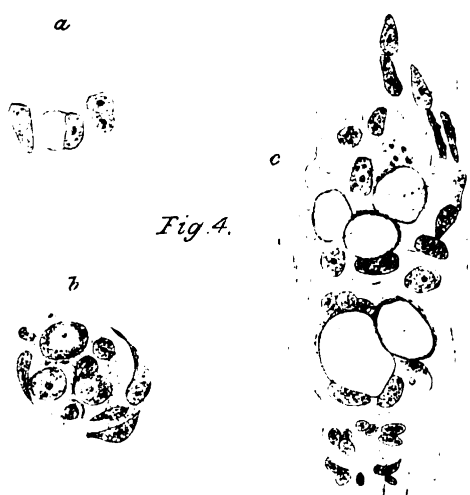


Fig. 4.

T. P. Collings

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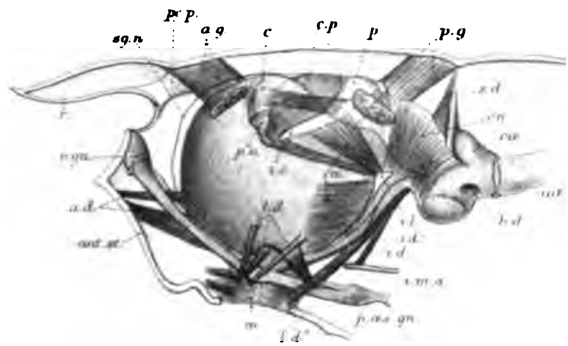

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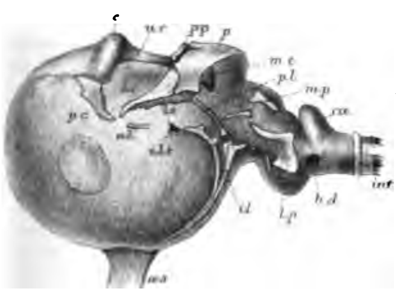

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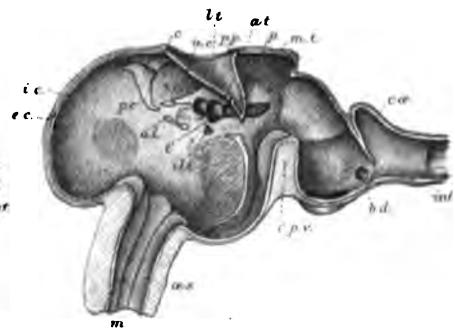

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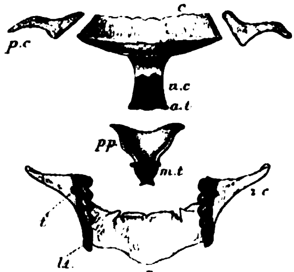

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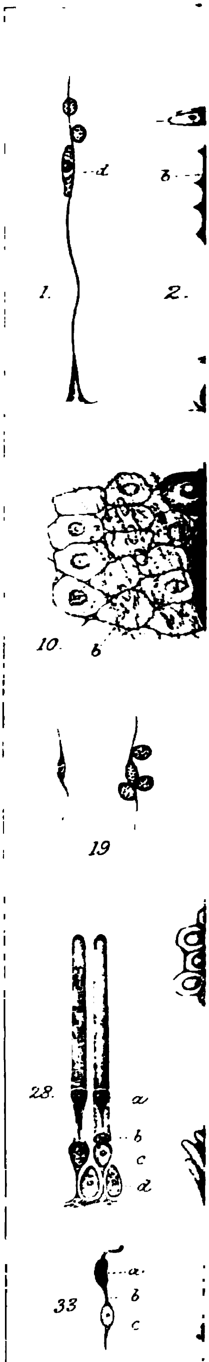

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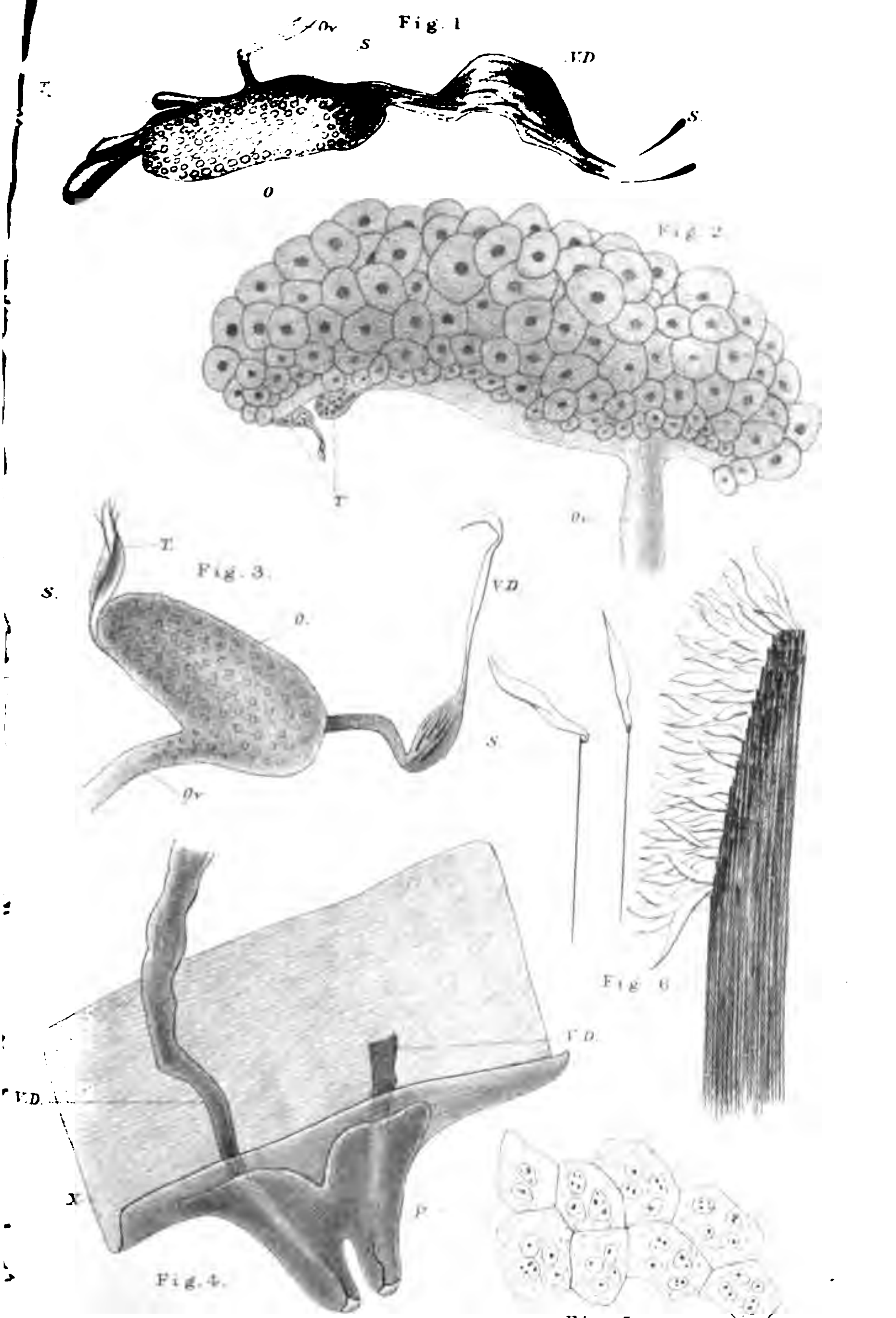

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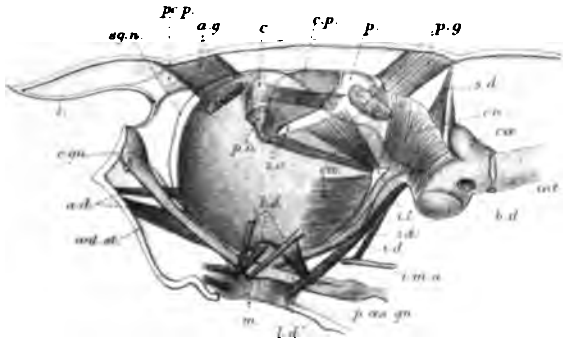

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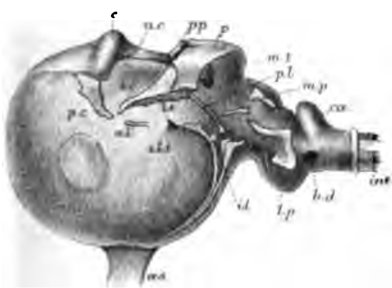

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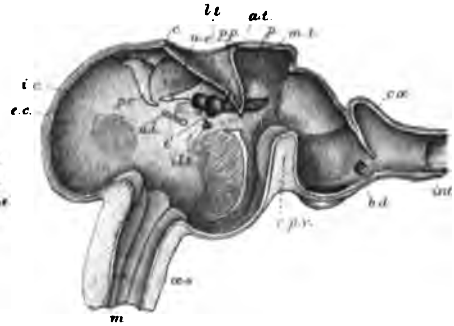

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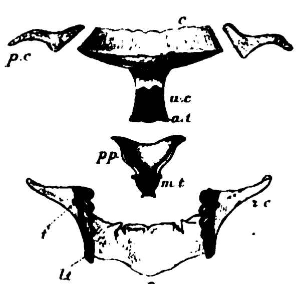

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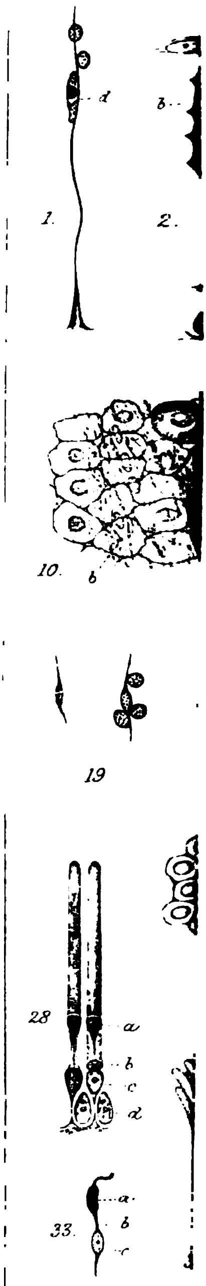

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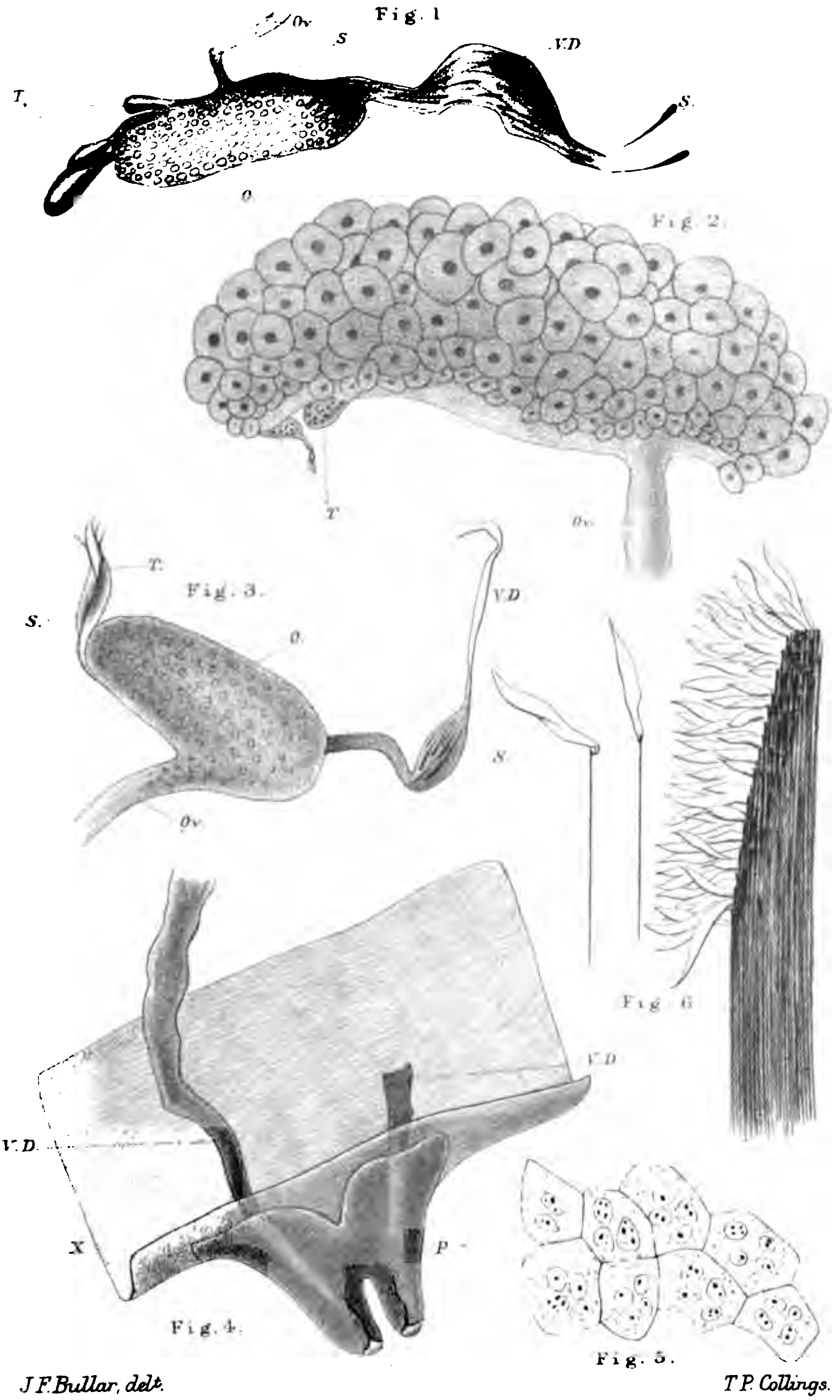

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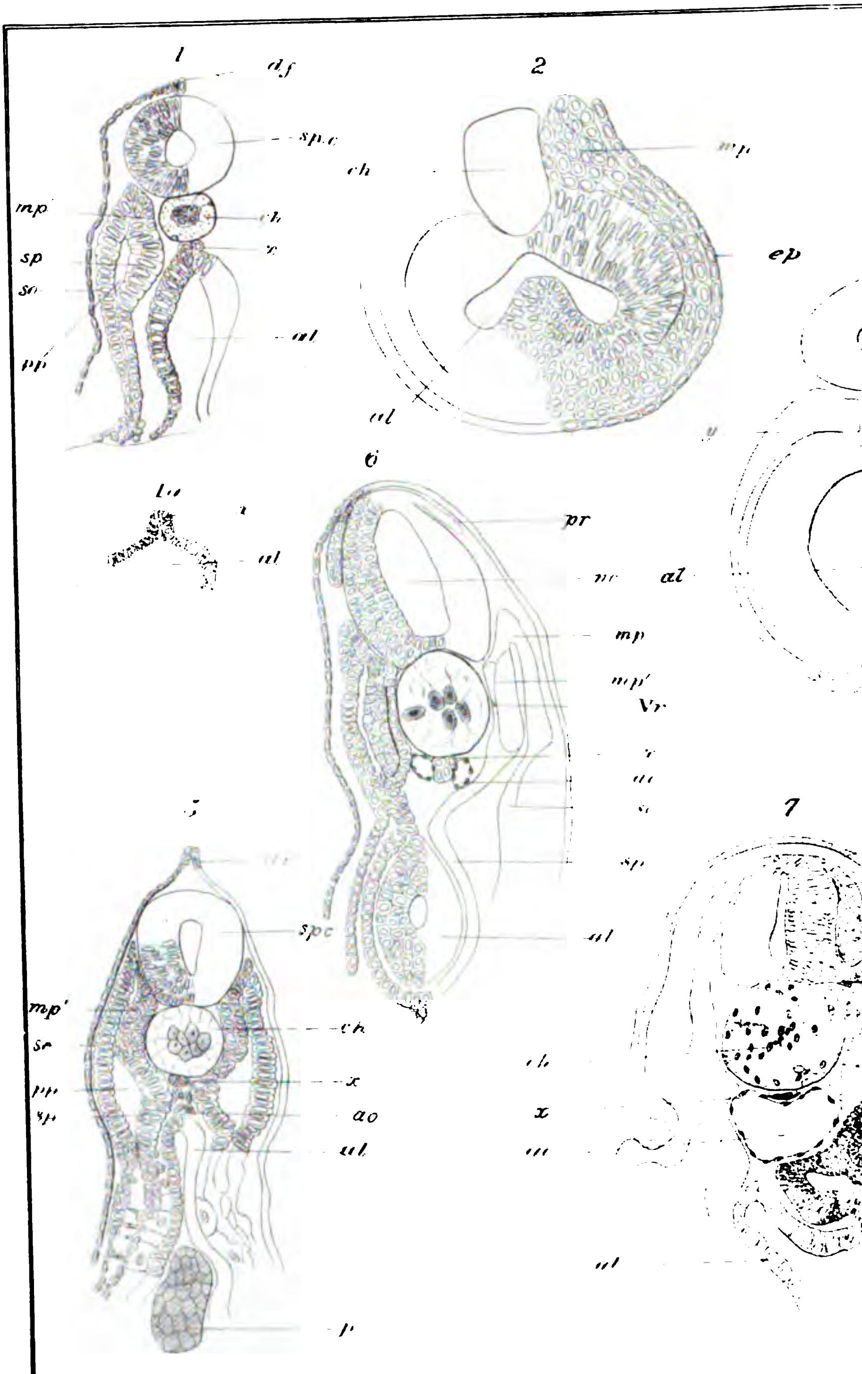

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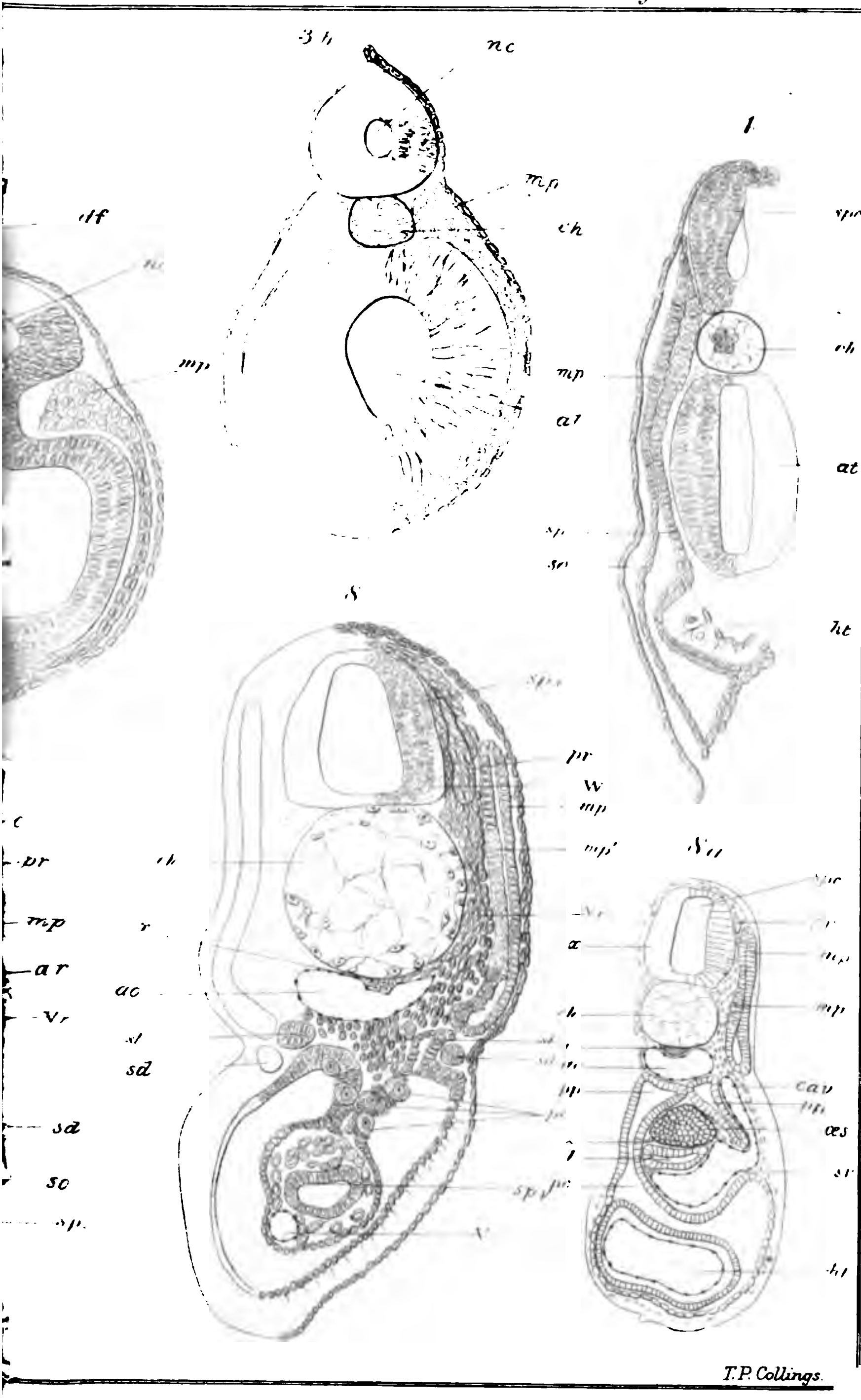
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T.P. Collings.

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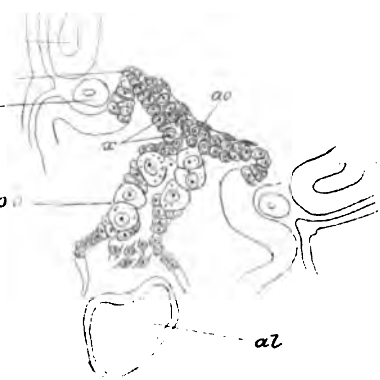

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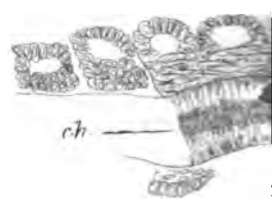

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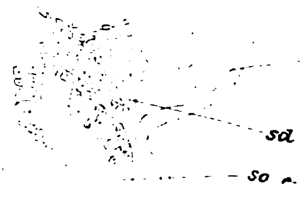

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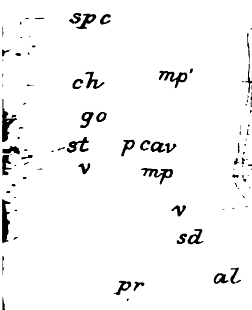

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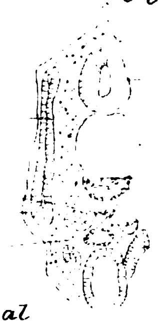

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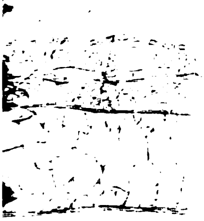

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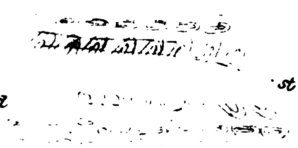

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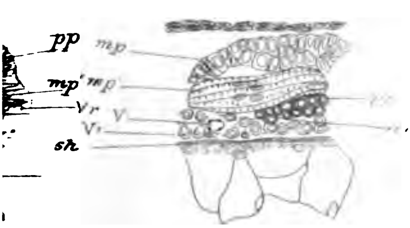

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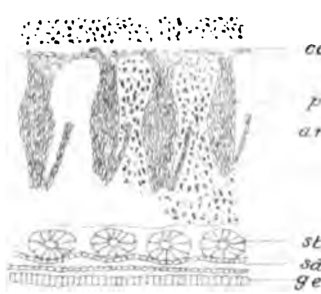

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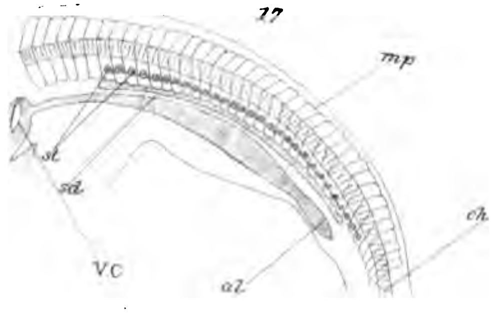

T.P. Collings.

Journal of Anatomy and Physiology.

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But little has been written on the spinal nervous system of the Cetacea. W. Rapp (*Die Cetaceen* Stuttgart, 1837) states "with respect to the course of the spinal nerves (of the Cetacea) there are no researches;" and Stannius simply mentions[1] that "in the dolphin a nerve-trunk proceeds out of the lumbar plexus, the branches of which are intended for the muscles of the rudimentary pelvis, and for the external genital organs and their muscles, as well as for the region of the anus:" Mr Swan, in the introduction to his work upon *The Comparative Anatomy of the Nervous System* published in 1835, has a short account of the whole nervous system of the Porpoise, and considering the limited space which he gives to it in his book, one cannot help admiring, notwithstanding the brevity of his description, the amount of information which he conveys on the subject. The investigations I have made will, I hope, very materially extend our knowledge of this subject, and I have taken care to have the more important of my dissections illustrated by drawings, whilst he, with his wealth of plates of the nervous system of other animals, does not give one to the Cetacea.

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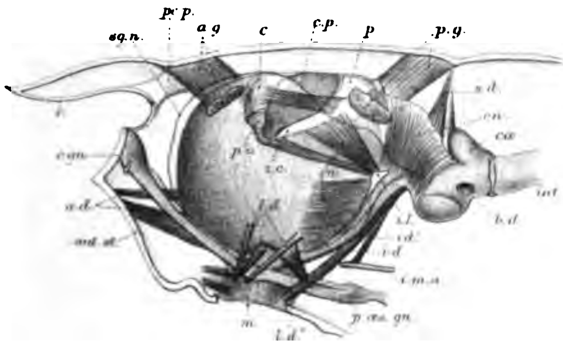

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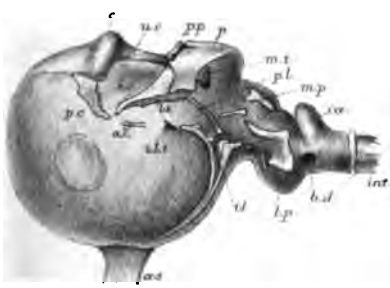

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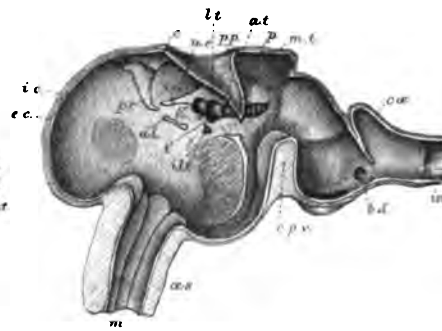

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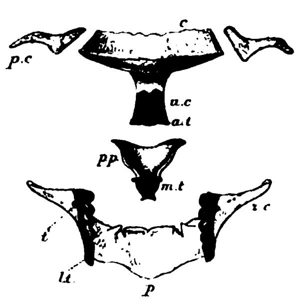

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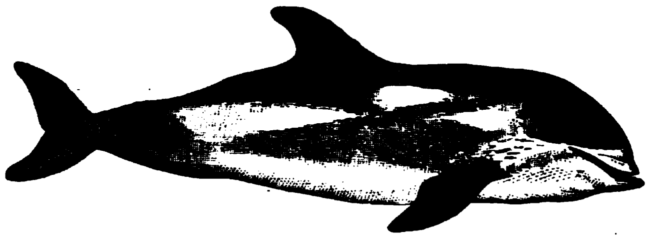

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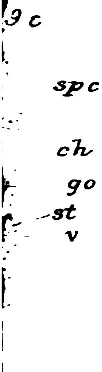

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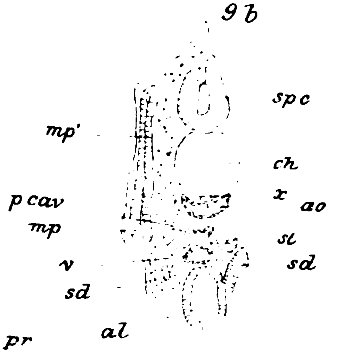

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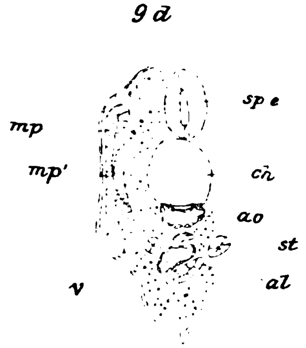

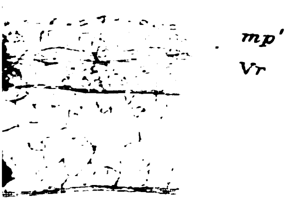

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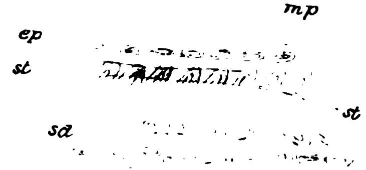

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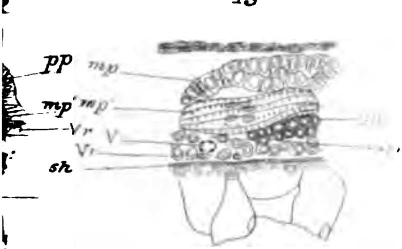

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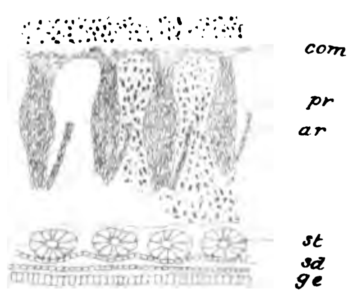

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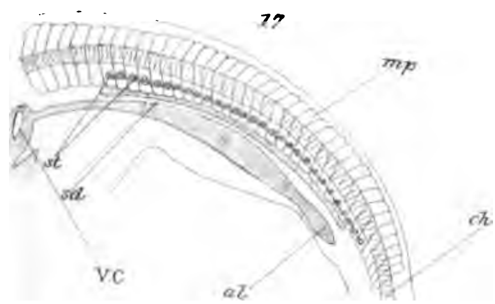

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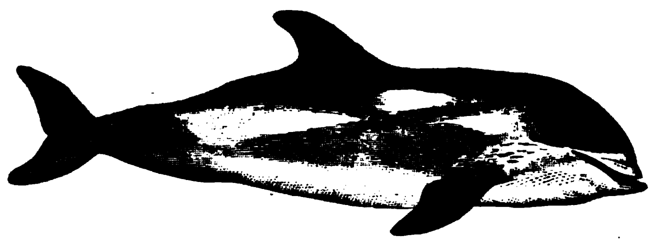

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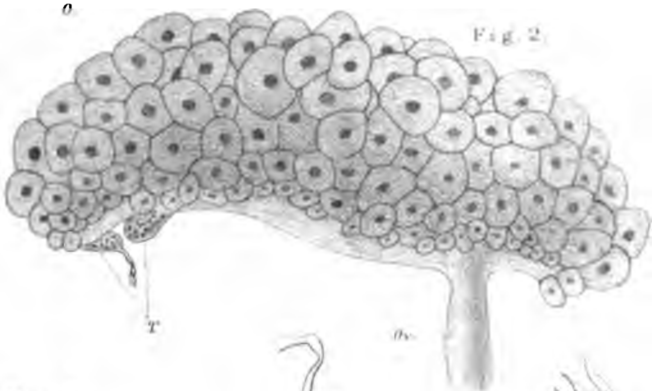

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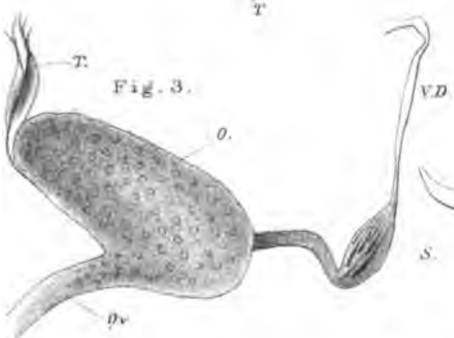

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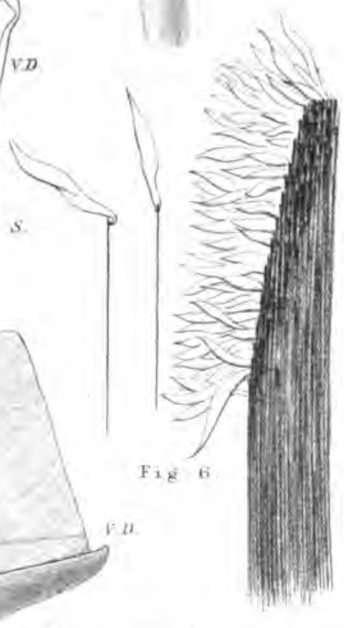

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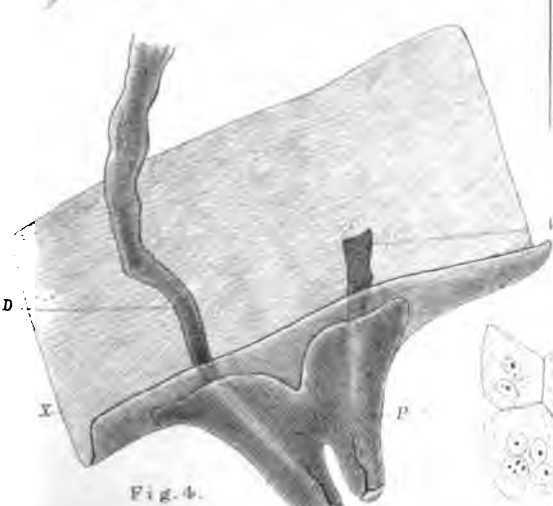

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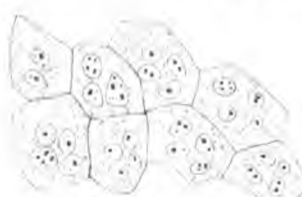
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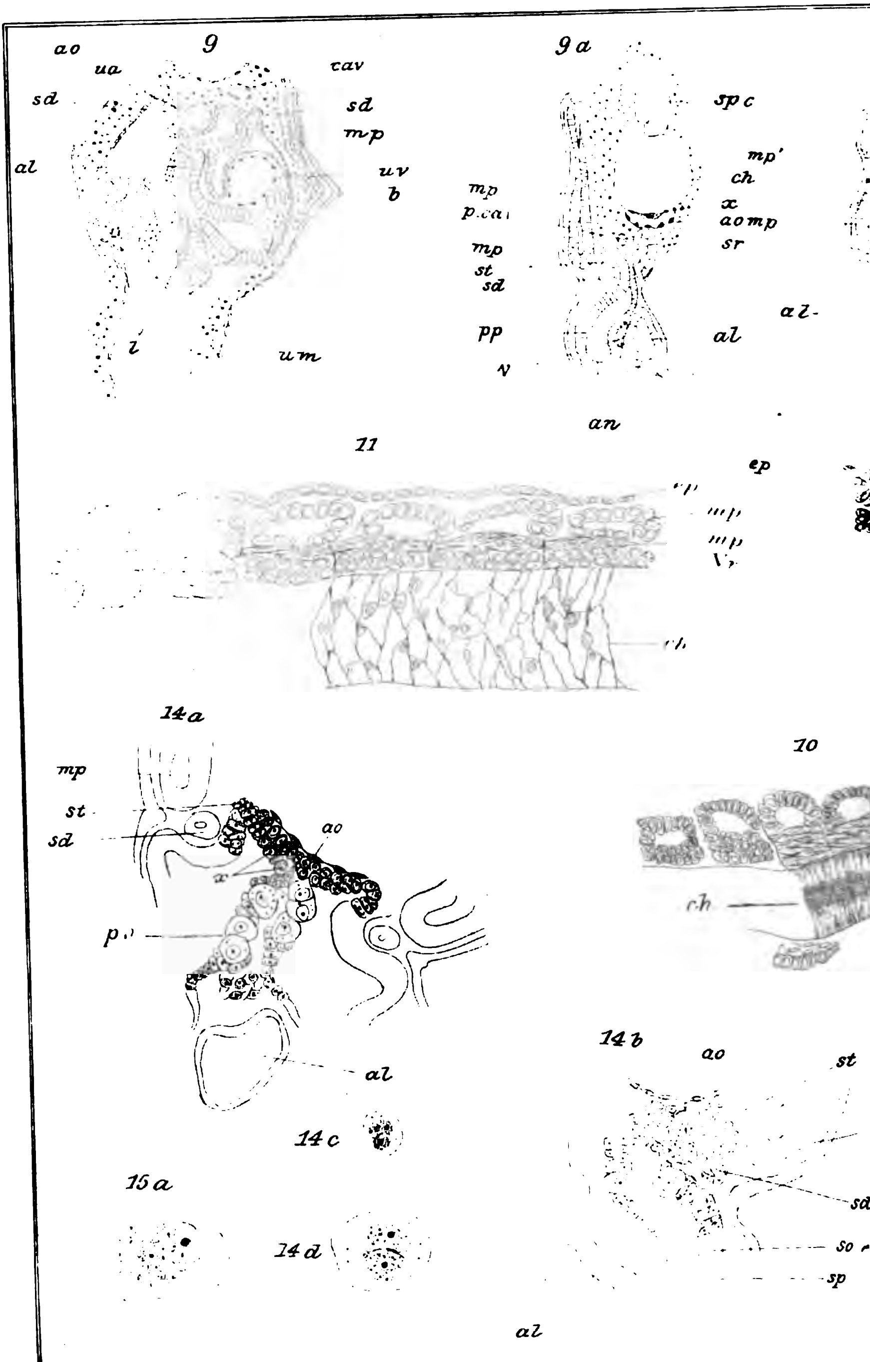
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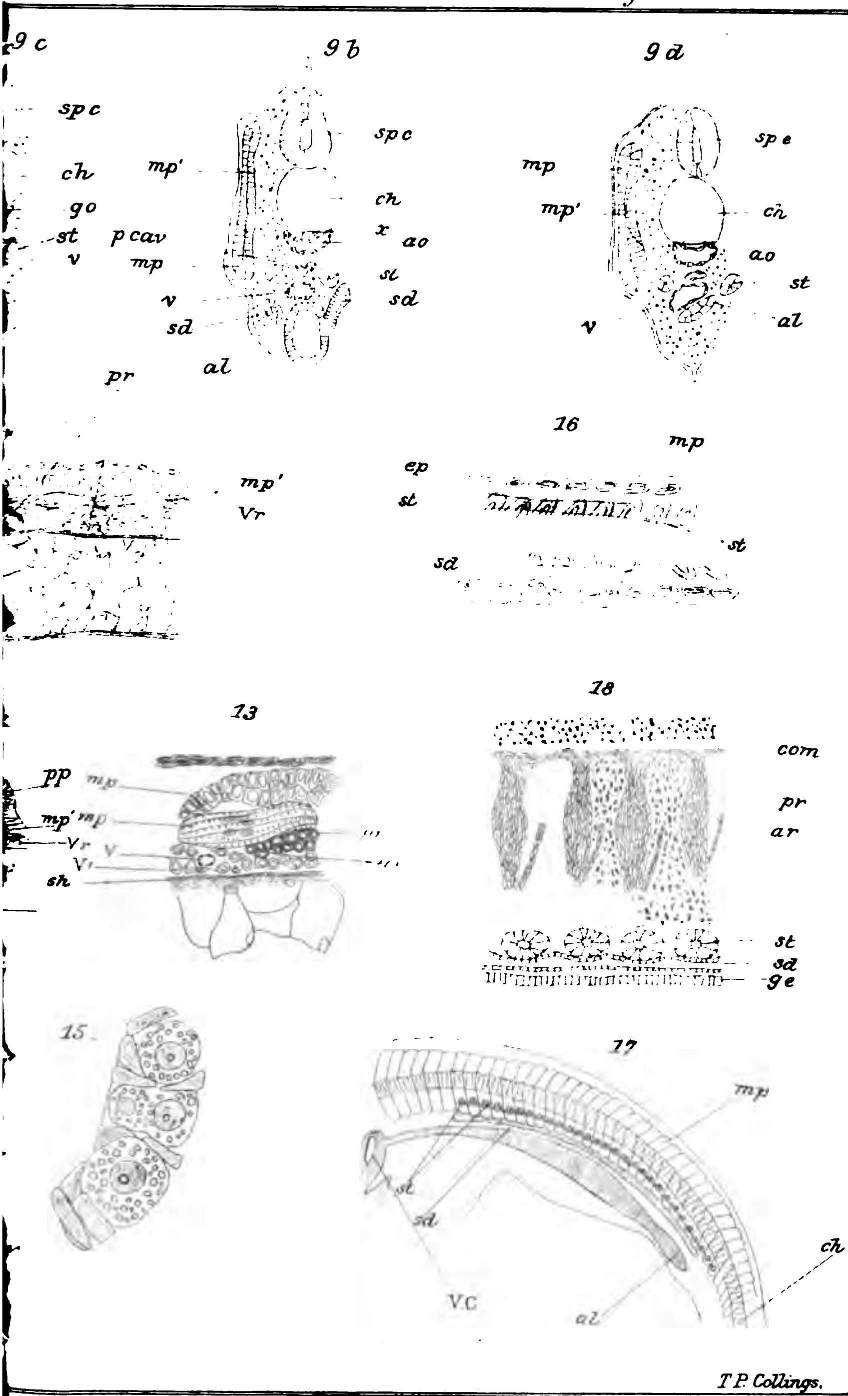
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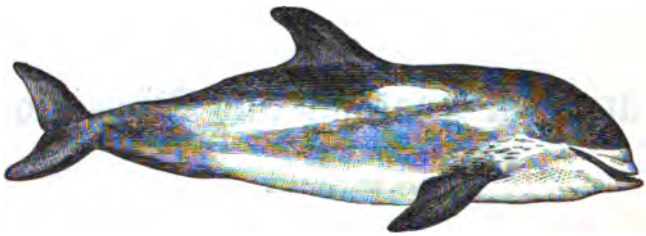

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ganglia, vary in the different regions of the spine. In the cervical region (*C.*) the roots are crowded together owing to the fusion or close apposition of the cervical vertebræ. The first three pass directly outwards, but the other five have a slight obliquity forwards. In the dorsal region (*D.*) the roots are placed at considerable intervals from each other, and the anterior pass directly outwards, whilst the posterior have an obliquity backwards. Those proceeding from the lumbar enlargement (*L. C.*) are densely crowded around the lower end of the cord, and, passing directly backwards, they constitute the cauda equina, and occupy the spinal canal for a considerable distance behind the termination of the cord. In the cervical and dorsal regions the length of the nerve-roots increases gradually from before backwards, but in the lumbo-caudal region, as the cord only extends to the 7th vertebra of this region, the length of the roots increases rapidly from nerve to nerve, until the more posterior of the series attain a very great length indeed. The nerves constituting the cauda equina are loosely bound to each other by lax connective tissue, and they are very curly and tortuous, so that their length cannot be correctly estimated by measuring from the point where they issue from the cord to the foramina of exit. In the most anterior of the series the tortuosities are long and gentle, but in the most posterior they are numerous and minute[1].

In the cervical and dorsal regions, the ganglia on the superior roots are well marked, and are placed in the intervertebral foramina. In the lumbo-caudal region, however, and especially in the posterior part of it, the ganglia are very minute and lie in the spinal canal, in some cases at a considerable distance from the foramina of exit.

In all the regions the superior roots (*s. r.*) are smaller than the inferior (*i. r.*), thus constituting a marked contrast to other mammalia, in which as a rule the reverse of this arrangement holds good. Nowhere, however, is this difference in size so marked as in the cauda equina, in the last nerves of which the superior root is half the size of the inferior, and in some cases

[1] Dr Murie of London has suggested to me that this tortuosity of the nerve-roots is in all probability due to the great freedom of movement and flexibility possessed by the caudal portion of the animal. I think that this view offers a very reasonable explanation.

so delicate that when stripped of the loose connective tissue which surrounds it, it resembles (in the porpoise) a fine thread or hair. From this fact we must not conclude that sentiency is dull in the Cetacea, for, as the animal tapers towards the tail, the amount of skin to be supplied with sentient fibres is small in comparison to the huge muscular masses to be supplied with motor filaments. In the cervical, dorsal, and anterior lumbar regions where the cutaneous surface is extensive, the superior roots attain a size only slightly smaller than the inferior roots.

SPINAL NERVES.—If we examine the spinal column of a porpoise or other cetacean, we notice that the intervertebral foramina, through which the spinal nerves pass, occupy different horizontal planes in the different regions of the column. This is owing to the absence of a pedicle in the lumbar and caudal regions of the column. Here the transverse processes spring from the sides of the vertebral bodies apart from the laminæ, which arise from the superior aspect of the bodies. In these regions, therefore, the intervertebral foramina correspond to the intervals between the laminæ of contiguous vertebræ, and consequently occupy a plane superior to the transverse processes. As we approach the dorsal region, however, a rudimentary pedicle begins to shew itself, the transverse process and lamina springing from the same point in the vertebral body, and the pedicle becomes more and more marked as we pass on towards the cervical region. In the cervical and dorsal regions, therefore, the intervertebral foramina are in a plane nearer the ventral surface, and are situated between the pedicles and inferior to the transverse processes.

In consequence of this arrangement the removal of the great extensor muscle in the lumbo-caudal region displays the whole spinal nerve issuing from the spinal canal, whilst in the dorsal and cervical regions it only exposes the superior divisions of these nerves passing upwards between the pedicles.

CERVICAL NERVES. (Fig. 2.)—In the cervical region the intervertebral foramina, as we have seen, are situated below the transverse processes of the vertebræ, and to expose the cervical nerves before they break up into their superior and inferior divisions, the dissection must consequently be made from the ventral aspect.

The cervical nerves are eight in number. The first, or suboccipital, passes out between the occiput and atlas, and is placed at a short distance from the second nerve. Owing to the fusion or close apposition of the vertebræ in this region, the other nerves lie very close to each other, being merely separated by the thin sharp osseous lamellæ which bound the intervertebral foramina and represent the pedicles. Outside the foramina the nerves are further separated from each other for a very short distance, by fibrous septa interposed between them and attached to the sharp margins of the lamellæ.

In form the cervical nerves are flat and band-like, and almost immediately after passing through the intervertebral foramina they divide into their superior and inferior divisions. The rete mirabile surrounding the cord is prolonged out with the nerves for a short distance, and forms for them a soft yielding bed outside the spinal canal.

Superior Primary Divisions of the Cervical Nerves (Fig. 2, *S. D.*).—These, with the exception of the superior division of the suboccipital, which is directed forward, pass upwards and backwards to end partly in the muscles and partly in the skin on the superior aspect of the neck. In some cases communicating branches of great tenuity pass between them close to the vertebræ, shewing even in this region a tendency to a plexiform arrangement, and the formation of a longitudinal cord along the superior aspect of the vertebræ. In the dolphin these communications are present in almost every case, but I have always failed to find them in the porpoise. In the substance of the great mass of muscle, through which the superior divisions pass, they break up into numerous branches which join freely with each other.

Inferior Divisions of the Cervical Nerves (Fig. 2).—These appear at the side of the neck, and are each connected with the sympathetic system by means of a delicate fasciculus. From the manner in which they communicate, the one with the other, they may be divided into a cervical, and a brachial or axillary plexus.

CERVICAL PLEXUS.—The cervical plexus is formed by the inferior divisions of the first *three* cervical nerves. These lie upon the inferior scalene muscle, and are at first under cover of

the splenius capitis, levator anguli scapulæ and superior scalene muscles. The second nerve sends a loop of communication under the transverse process of the atlas to the first nerve, and receives a similar loop at a lower level from the 3rd nerve.

The branches of this plexus may be divided into (1) musculo-cutaneous or superficial, (2) muscular, (3) communicating.

Musculo-cutaneous branches, (*c.*)—These are three in number, and they spring from the 2nd and 3rd nerves. Crossing the inferior scalene muscle, the upper two pass superficially to the mastoido-humeral muscle, and then break up into their branches of distribution. The third and lowest, after receiving a reinforcing twig from the loop of communication which joins the 2nd with the 1st cervical nerve, pierces the mastoido-humeralis, giving it at the same time a twig of supply, and then breaks up into branches. On tracing the branches of these three nerves, we find that some spread upwards and forwards to supply the skin over the auricular and posterior part of the infra-maxillary region, whilst others proceed downwards and forwards to the cutaneous muscle and skin of the throat. These nerves correspond to the superficial branches of the cervical plexus in man.

Muscular branches.—From the 1st and 2nd nerves proceed numerous branches (*m. b.*) to the muscles of the neck, and two nerves (*s. a.*) of considerable size may be traced, the one from the 2nd, and the other from the 3rd, to the inferior scalene muscle. The principal muscular branch of the cervical plexus, however, is the phrenic (*p.*). This nerve is derived from the 3rd and passing downwards, over the scalenus inferior, it is reinforced by a twig (sometimes of considerable size) from the 4th and 5th nerves. Reaching the lower margin of the inferior scalene muscle it takes this as its guide and curves backwards under the brachial plexus, and enters the thorax. Before doing so, however, it gives a branch (*c. s.*) to the costo-scapular muscle. Within the thorax we trace it upon the pericardium and under cover of the pleura to the diaphragm. In its course it gives a few delicate filaments to the pleura and pericardium.

Communicating branches.—The 1st cervical nerve or suboccipital, after being joined by the loop of communication from the 2nd cervical nerve, proceeds downwards across the inferior

scalene muscle, and passing under the posterior margin of the sterno-mastoid muscle it joins the large descendens noni branch (*d. n.*) of the hypoglossal nerve (*h.*)[1].

Brachial Plexus (Fig. 2).—The brachial plexus is formed by the union of the inferior trunks of the five posterior cervical and 1st dorsal nerves. In some cases it is further reinforced by a slender fasciculus from the 2nd dorsal nerve. These nerves emerge from under cover of the superior scalene muscle, and lying upon the inferior scalene they are in relation to the deep aspect of the muscles which clothe the venter scapulæ. The manner in which they unite to form the plexus is somewhat variable.

In the porpoise (Fig. 2), the 4th and 5th nerves join to form an anterior cord (*A.*), the 6th and 7th to form a second or median cord (*M.*), and the 8th and 1st dorsal to form a third or posterior cord (*P.*). The anterior cord next forms a junction with the median cord, and the union of this trunk with the posterior cord constitutes the plexus.

In the dolphin the 4th, 5th and 6th nerves lying parallel and very close to each other unite to form one cord, whilst a second cord is formed by the junction of the 7th and 8th with the first dorsal and a small fasciculus from the 2nd dorsal. The first cord after giving off several branches joins the second cord, and by their union the plexus is formed. It is curious to find a twig from the 2nd dorsal entering into the formation of this plexus. This little filament passes forwards and slightly downwards under cover of the two anterior ribs, and joins the 1st dorsal as it emerges from under cover of the first rib.

The branches of the brachial nerves are as follows (Fig. 2):

From the 4th nerve a branch of considerable size is given to the inferior scalene muscle (*s. a.*). This muscle is therefore richly supplied with nerves, which are derived from three sources, for, in addition to the branch in question, it receives, as we have already seen, other two distinct nerves, one from the 2nd and the other from the 3rd cervical nerve (*s. a.*). *From the*

[1] The nerve thus formed is somewhat larger than the hypoglossal itself and emerging from under the anterior or lower margin of the sterno-mastoid it breaks into numerous branches, the most of which enter the large fleshy mass which corresponds to the sterno-hyoid, whilst a few small twigs may be traced to the sterno-thyroid and one very delicate filament to the thyro-hyoid.

7th nerve some twigs are given to the scalenus superior muscle. *From the anterior cord* proceed two nerves; of these one goes to the subscapularis muscle (*s.*), whilst the other—much the larger of the two—is the suprascapular (*s. s.*) and supplies the spinatus muscles.

From the brachial plexus branches are supplied to the subscapularis (*s.*), teres major, serratus magnus, latissimus dorsi, pectoralis major, costo-scapular and to the panniculus carnosus (*p. c.*); also some cutaneous branches which issue from under cover of the axillary border of the scapula and latissimus dorsi, and ramifying on the deep surface of the cutaneous muscle, pierce it to reach the skin. The principal branches of the brachial plexus, however, are the medio-ulnar, the musculo-spiral and the circumflex.

Medio-ulnar nerve (*m*).—This is a large nerve which proceeds to the palmar aspect of the flipper. About the level of the elbow-joint it gives two well-marked branches (*u.*) to the ulnar margin of the forearm, and these being in all probability the representatives of the ulnar nerve I have been led to apply the name of medio-ulnar to the parent trunk. In the forearm it lies in the groove between the ulna and radius, and gives numerous fine twigs to the skin on the palmar aspect of these bones; then crossing the carpus in the middle line of the flipper it enters the phalangeal region of the manus. Here it is placed deeply in the interval between the index and middle fingers and can be traced almost to the tip of the flipper. In this part of its course, it gives numerous twigs to the skin, and a few very delicate filaments may be followed out between the phalanges to the dorsal aspect.

Musculo-spiral nerve (*m. s.*).—This nerve at a short distance from its origin gives a branch of considerable size to the ulnar side of the palmar aspect of the forearm, and then winding round the lower end of the humerus through a triangular space formed by the triceps, teres major and humerus it reaches the dorsal aspect of the flipper. (Fig. 3, *m.*) Here it breaks up into numerous slender branches which spread out to supply the skin on the ulnar side of the upper arm and forearm. One or two of these twigs may be traced as far as the carpus, but apparently they do not extend further. As the nerve passes

through the triangular space it gives a branch of supply to the triceps muscle.

Circumflex nerve. (Fig. 2, *a.*)—This nerve has a very important and extensive distribution. After giving a few small twigs to the teres major, it hooks round the posterior or axillary border of the subscapularis muscle, and passing through a quadrilateral space formed by the triceps, teres major, humerus and scapula, it reaches the dorsal aspect of the latter bone and divides into two branches. (Fig. 3, *c.*) The upper of these, after giving a small cutaneous nerve (*c. s.*) to the skin over the shoulder-joint, breaks into numerous branches (*d.*) which sink into the substance of the deltoid muscle. The lower branch, passing under cover of the deltoid near its insertion, is continued downwards, and emerging on the radial side of the dorsal aspect of the humerus it gives cutaneous filaments to the skin of this region, as well as to that over the elbow-joint, whilst a few twigs may be traced to the skin over the radius.

But in addition to these large nerves of the flipper there is yet another branch (Fig. 2, *i. c.*) of small size, which springing from the deep aspect of the brachial plexus, passes downwards to supply the skin on the palmar surface of the upper arm and upper part of the forearm. From the fact that it is somewhat more liberal in its distribution of branches to the ulnar than to the radial side of the flipper, I am inclined to think that this nerve is the representative of the internal cutaneous.

The description which I have given of these nerves does not coincide with the brief account given of them by Swan in his work upon *The Comparative Anatomy of the Nervous System*, and it is only after the most careful study of my several dissections that I venture to differ with so distinguished an anatomist. It may be as well that I should point out wherein we disagree. In his description he states that from the brachial plexus there proceeds a nerve similar to the musculo-spiral, also an ulnar and a small median, and he affirms that there is no circumflex, neither an internal nor an external cutaneous. Now the nerve which I take to be the median (medio-ulnar)—and I think that its position in the middle line of the palmar aspect of the flipper bears me out in my

opinion—is as large, if not larger, than any of the others, and has in some respects a more extensive distribution. The ulnar, on the other hand, is only represented by the branches which proceed from this nerve to the ulnar side of the forearm, and also by another branch having a similar distribution which springs from the musculo-spiral. That a well-marked circumflex is present will, I think, be at once apparent by the study of the course of the nerve to which I have given this name, and also from the fact that its main distribution is in the substance of the deltoid muscle. It is satisfactory to find, however, that I am supported on this point by the evidence of Carte and Macalister, who incidentally mention (*Phil. Trans.* Vol. CLVIII. 1868, p. 200) that, in the course of their dissection of the muscles of the *Balaenoptera rostrata*, they observed the circumflex nerve with the accompanying artery passing through the usual quadrilateral space.

DORSAL NERVES.—The dorsal nerves equal in number the dorsal vertebræ. In the costal region of the vertebral column the foramina through which the spinal nerves pass occupy different planes in the anterior and posterior parts. In describing the superior divisions of the dorsal nerves, therefore, it will be convenient to deal first with those in the anterior part of the region, and then with those in the posterior.

Superior Primary Divisions of the Dorsal Nerves.—In the anterior dorsal region the superior divisions of each of the spinal nerves, on reaching the upper surface of the vertebral laminæ, divide into three branches:—(1) A well-marked external branch, which, following the course of the transverse process of the vertebra posterior to it, passes directly outwards to supply the skin covering the back, giving, at the same time, however, several branches to the extensor muscle. (2) An internal branch, which runs upwards and inwards in the direction of the spinous processes. This nerve is chiefly for the supply of the great mass of muscle through which it passes, but a few filaments reach the skin. (3) An extremely slender communicating branch, which, passing over the vertebral lamina, joins the superior division next in order. These connecting links between the various superior divisions are not present in every case, and can only be discovered by very careful dissection.

In the posterior dorsal region the removal of the extensor muscle displays the spinal nerves dividing into their superior and inferior divisions.

The superior divisions give off well-marked communicating branches which, passing over the laminæ, connect the various superior trunks with each other. Here therefore the great superior longitudinal plexus or cord, so characteristic of the Cetacea, may be considered to begin. In the cervical and anterior dorsal regions a tendency to a similar arrangement is shewn, but only towards the middle of the dorsal region is it thoroughly established.

Fig. 6.

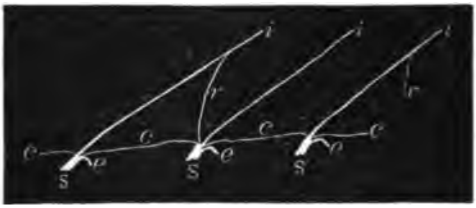


Diagram of the superior divisions of the spinal nerves in the posterior part of the dorsal region. *S.* superior divisions. *e.* external branches. *c.* communicating branches. *i.* internal branches. *r.* reinforcing twig to the internal branch.

The internal and external branches of the superior divisions are well marked, and similar in their distribution to those of the anterior part of the region. The internal branch, however, is in many cases reinforced by a fasciculus which comes off from the superior trunk next in series.

Inferior Primary Divisions of the Dorsal Nerves.—These nerves are accompanied outwards for some distance by processes of rete mirabile prolonged through the intervertebral foramina. The greater portion of the first nerve, and likewise, in some cases, a slender fasciculus from the second, enter into the formation of the brachial plexus. In their course towards the inferior aspect of the animal, the inferior divisions of the dorsal nerves accompany the intercostal blood-vessels and constitute the intercostal nerves. At first they lie upon the pleura, but afterwards they pursue their way downwards between the intercostal muscles. In their distribution they are similar to the same nerves in other mammals. They give small lateral cutaneous twigs and branches of supply to the

intercostal muscles. The anterior three or four end in the triangularis sterni muscle, whilst the others are continued on between the abdominal muscles, which they supply, to end in minute terminal twigs to the skin of the belly.

LUMBO-CAUDAL NERVES. (Fig. 4.)—The arrangement of the spinal nerves posterior to the dorsal region is different from that of any other group of mammals (excepting perhaps the Sirenia), with which I am acquainted. The final cause of this is obvious; it is an adaptation of the nervous system to meet peculiarities in the muscular construction of these animals. In other mammals powerful inferior or posterior extremities are developed for the purpose of locomotion, and consequently the inferior divisions of the lumbar and sacral nerves are large, and thrown into plexuses to supply the muscles which act upon these limbs. In the Cetacea, on the other hand, lower limbs are absent, so far as locomotion is concerned. The tail is the great organ of locomotion, and the muscles which work it are developed equally above and below the transverse processes of the vertebral column—the former constituting the great extensor, and the latter the great flexor muscle of the tail. In consequence of this, the superior divisions of the spinal nerves have as important a part to play in the supply of the muscles of the chief organ of locomotion as the inferior, seeing that it falls to them to give branches to the extensor muscle, whilst the latter have as their office the supply f the flexor muscle. The result of this is, that the superior and inferior divisions of the lumbo-caudal spinal nerves in the Cetacea are very nearly of equal size.

To insure the proper nervous supply of these great muscular masses, two large longitudinal cords or trunks are formed by the spinal nerves, on each side of the vertebral column—one superior and formed by the junction of the various superior divisions, and the other inferior and formed by the union of the inferior divisions. The first of these commences, as we have already seen, in the middle of the dorsal region, but even in the anterior dorsal and cervical regions a tendency to a similar arrangement is exhibited. The inferior longitudinal cord begins further back at a point corresponding to the 11th lumbo-caudal vertebra. Posterior to this point, therefore, we

have four large nervous cords arranged parallel to the vertebral column—two of which are superior and situated one on each side of the vertebral spines, and two inferior and placed one on each side of the vertebral bodies below the transverse processes. They are continued back to the tail, and their chief function is to supply the four great muscular masses which act upon the tail. Sensory filaments, however, are also given to the skin.

So much for the general arrangement of the lumbo-caudal spinal nerves. It remains for me to describe their more special distribution.

In the porpoise the lumbo-caudal nerves are twenty-five in number on each side, and they issue from the spinal canal by passing upwards between the laminæ on a plane superior to the transverse processes. By removing the extensor muscle, therefore, they are displayed dividing into their superior and inferior divisions. We will first follow out the superior divisions.

Superior Primary Divisions of the Lumbo-caudal Nerves. (Fig. 4.)—In the anterior part of the lumbo-caudal region the superior divisions of the spinal nerves have an arrangement very similar to that exhibited in the posterior dorsal region. Each trunk gives off a well-marked communicating branch, which, joining the superior division next in order, forms and continues back the longitudinal plexus. This, as we trace it backwards, assumes more and more the character of a large nervous cord, and the further we follow it the greater becomes the proportion of fibres it receives from each superior division, until the greater part of these nerves enter it. The last joins it at a point corresponding to the interval between the 25th and 26th lumbo-caudal vertebræ.

The cord (*N*) thus formed is of a considerable size and is at first situated upon the laminæ of the vertebræ; afterwards, however, it lies upon the vertebral bodies. It is flat and band-like in form and its nerve-fasciculi are held very loosely together; indeed it has the appearance of being composed of a number of small nerves running parallel to each other and held together by a small amount of lax connective tissue.

As it passes onward towards the tail, from the point at

which the last superior division joins it, it gradually diminishes in size, owing to the various fasciculi of which it is composed leaving it in the form of nerves. For a short distance anterior to the tail, and in the tail, it lies between the extensor tendons and in a tube of dense fascia, which is attached to the vertebral bodies.

Branches.—Anterior to the 18th lumbo-caudal vertebra the branches which are given off by the superior longitudinal plexus are similar to those we have seen coming off from the superior divisions in the posterior dorsal region, but they differ somewhat in their distribution. *The internal branches* (*a.*) have an oblique direction inwards and backwards towards the spinous processes, and they supply the skin and muscles of the back. Opposite the dorsal fin, where the cutaneous surface is more extensive, the internal branches are slightly larger than elsewhere. Each internal branch receives as a rule a reinforcing twig (*b.*) from the superior division next in series. *The external branches* (*e.*) are very numerous, and frequently two or even more proceed from each superior division, or from the cord at the point where this enters it. They are directed outwards and backwards and are mainly destined for the supply of muscle. In addition to these there is frequently to be seen a slender twig which passes obliquely outwards over the transverse process to end in the skin.

Posterior to the 18th lumbo-caudal vertebra the branches are not so numerous, and they come off directly from the cord and not necessarily from the point at which the superior division enters. The internal branches receive no reinforcing twigs, are very long and oblique in their course, and continue backwards alongside of the cord for a considerable distance before diverging to attain their various points of distribution. The external branches are also few in number and small in size.

If we now trace the superior longitudinal cord into the tail we find that it continues back in a straight course close to the middle line and is lost near the notch in the posterior margin of the tail. It gradually diminishes in size by giving off slender twigs (*R*) from its outer edge to the skin on the superior aspect of its own side of the tail. These are very numerous, and can

only be traced outwards for a short distance owing to the dense tissue through which they pass. In the diagram they are exaggerated both in length and size.

Inferior Primary Divisions of the Lumbo-caudal Nerves (Fig. 4, *d.*).—These run outwards and downwards over the intervertebral discs and disappear between the transverse processes. To expose them further the transverse processes require to be snipped through with the bone-pliers close to their roots and removed. This is the method I adopted in the dissection figured in Fig. 4.

The first eleven of the inferior divisions of the lumbo-caudal nerves correspond to the lumbar and sacral nerves in man, but they do not join in such a manner that we can divide them into two distinct plexuses—a lumbar and a sacral.

As they pass between the transverse processes each of the anterior seven nerves gives off a well-marked branch which, joined by a twig from the sympathetic (*P*), communicates with its fellow branches in such a way as to form a series of loops under the transverse processes. Some filaments pass from this into the substance of the flexor muscle. The main trunks then pass onwards into the substance of the flexor muscle, and there they communicate with each other in a plexiform manner. The four anterior nerves, piercing and giving numerous branches to this muscle, are continued on to the inferior aspect of the animal between the abdominal muscles, and end partly in muscle and partly in skin. The remaining three nerves, curving backwards in the substance of the flexor muscle, terminate in it.

We may compare the distribution of these nerves to that of the ilio-hypogastric, ilio-inguinal, and the muscular branches to the psoas muscle in the human body.

The 8th, 9th and 10th lumbo-caudal nerves, with a large branch from the 11th, and anteriorly a minute twig from the 7th, unite to form the genital or internal pudic nerve (*M*). The 8th, 10th and 11th likewise each give one or two twigs to the flexor muscle. But as there is no lower limb, the branches corresponding to the genito-crural, obturator, external cutaneous, anterior crural, and sciatic are absent. The internal pudic is well represented.

Internal Pudic or Genital Nerve.—This is a very large nerve. It pierces the flexor muscle and, giving off no branches

Fig. 7.

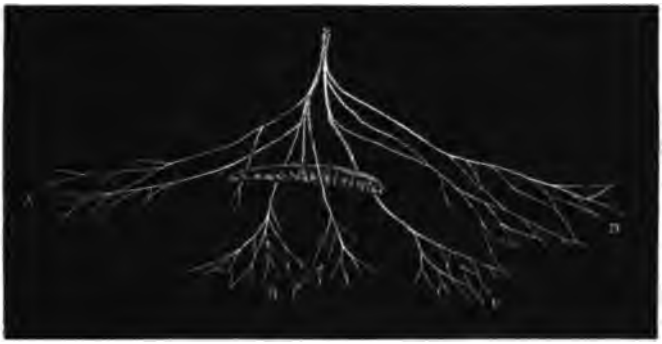


Diagram of the internal pudic nerve. *p.* pelvic bone. *A.* branches to region of anus. *B.* to labia majora and mammary gland. *C.* to clitoris. *D.* to vagina and bladder.

on the way, it emerges at the level of the pelvic bone, and immediately divides into two divisions from which its numerous branches proceed.

In the female two or three slender branches pass backwards to supply the muscles connected with the anus and the surrounding skin. Others, directed forwards, ramify on the vaginal wall and bladder and there communicate with sympathetic filaments from the hypogastric plexus. A large branch, taking a deep course under cover of the pelvic bone, can be traced into the clitoris, whilst others, also under cover of the bone, supply the genital muscles attached to it. Two or three branches of good size pass superficially to the pelvic bone, and end, some in the mammary gland, and others in the skin of the labia majora. I have not had an opportunity of dissecting this nerve in the male, and consequently cannot give an account of its distribution.

From the 11th lumbo-caudal nerve backwards all the inferior divisions join to form the inferior longitudinal cord or plexus (*O*) which soon acquires a considerable size. In form and constitution it closely resembles the superior cord. At first it lies immediately below the transverse processes on the sides of the vertebral bodies, but as we trace it back we find that it gradually converges towards the middle line until it lies along

the under surface of the column. The last nerve enters it opposite the 26th lumbo-caudal vertebra, and from this point backwards it gradually diminishes in size.

Branches.—These are very numerous, and as a rule they come off from the points where the cord is joined by the various inferior divisions. They supply both muscle and skin, and are so variable that classification is impossible. Very frequently, as is seen in the diagram, they join in a complicated plexiform manner in the substance of the flexor muscle before proceeding to their various points of distribution. One branch, which comes off opposite each intervertebral disc, passes upwards between the next two transverse processes to end in the extensor muscle.

In the tail the inferior longitudinal cord lies between the flexor tendons, and ends by giving branches to the skin on the inferior aspect of its own side. Its distribution in the tail therefore is precisely similar to that of the superior cord on the superior aspect.

In Swan's work already quoted (p. xxx.) I find the following remarks upon the tail of the porpoise: "The large nerves of the tail exist more for conferring muscular power than sensation, and the portions reaching the broad flat surface on the extremity are very diminutive; it therefore appears that the tail is not only a powerful instrument for motion, but for defence, and that it is capable of giving hard blows without feeling much pain; it is therefore furnished with just as much nerve as will produce a moderate perceptiveness, something between that of skin and horn."

Whilst the dense, hard texture of the tail suggests the idea of a very *unfeeling* structure, I cannot believe that it is so very devoid of sentiency as to be compared, even for a moment, with horn. The nerves which supply it are not so "very diminutive;" they are four in number, and in a porpoise, 3 or 4 ft. in length, each is fully as large as the phrenic in man. The tail is doubtless a powerful instrument for defence, and is perhaps capable of giving hard blows with less pain than any other part of the body; but still to render it an efficient organ for progression, it must be possessed of a sentient function, capable of conveying to the nerve-centres an exact impression of how it stands in

relation to the water—the resisting medium against which it strikes.

The aquatic life of the cetacea and their close resemblance in external form to the fish naturally suggest the probability of there being many affinities in the anatomy of these two great classes of animals—more especially in the structure of their great propeller, the tail, and the apparatus which works it. With the object of ascertaining how far this is true in regard to the nervous arrangements, I have made several dissections of fish.

The spinal nervous system of the fish is arranged upon a totally different plan. The spinal cord is continued back to the tail, where it ends in a bulb. The spinal nerves are in the form of superior and inferior fasciculi, and each of these divides into two. One of the branches of the inferior division joins with one of the branches of the superior division, and the resultant nerve goes to the muscles and skin on the lower aspect of the vertebral column. The nerve which goes to the parts above the column is formed by the second branch of the inferior division, communicating with the first branch of the superior division, and then joining with the second branch of the superior division next in order.

From the spinal cord passing so far back in the vertebral canal it follows that the nerves which supply the caudal apparatus have a very short course to run from their points of origin to their distribution. Very different is the arrangement of the corresponding nerves in the cetacea, which spring from the lumbar enlargement at a point far in front of their areas of distribution. In the fish, therefore, there is no need for the longitudinal cords for the purpose of conveying the nerves to the caudal apparatus—the spinal cord itself is their substitute.

In the fish, however, the caudal region is not supplied by the spinal nerves alone. From the vagus nerve as it passes through the foramen in the lateral occipital bone one—sometimes two—nerves are given off. In the Haddock this branch reaches the surface at a higher level than the pectoral fin by passing outwards under the scapular arch. It is then continued back to the tail in the groove between the upper and lower masses of muscle and immediately beneath the skin, to

which it gives slender filaments. In the Skate it has different relations. It passes backwards under cover of the dorsal muscles and in contact with the spinal nerves, and it only becomes superficial in the caudal region. It gives twigs to both muscle and skin, but apparently does not communicate with the spinal nerves, although in close relation to them.

I do not consider that this nerve in the fish can be regarded as presenting any affinity to the caudal trunks of the cetacea.

EXPLANATION OF PLATE VII.

Fig. 1. Diagrammatic sketch of the spinal cord of the porpoise with the nerve-roots spread out. *C.* Cervical nerve-roots; *D.* Dorsal nerve-roots; *L.C.* Lumbo-caudal nerve-roots. The great length, and tortuosity of these may be observed. *ft.* The filum terminale; *sr.* Superior roots; *ir.* Inferior roots; it will be seen how large these are in comparison with the superior roots; *s.* Superior branch of the spinal nerve; *i.* Inferior branch of the spinal nerve.

Fig. 2. Cervical nerves of the porpoise. 1*C.* 1st cervical nerve; 8*C.* 8th cervical nerve; 1*D.* 1st dorsal nerve; *SD.* Superior divisions of the cervical nerves; *mb.* Branches to the muscles of the neck; *c.* The musculo-cutaneous branches which correspond to the superficial nerves of the cervical plexus in man; *h.* hypoglossal nerve; *dn.* Descendens noni; *sa.* Branches to the scalenus inferior; *p.* Phrenic; *cs.* Branch to costo-scapular; *A.* Anterior cord; *M.* Median cord; *P.* Posterior cord; *ss.* Suprascapular; *s.* Branches to the subscapularis muscle; *pc.* To panniculus carnosus; *t.* To teres major; *a.* Circumflex; *ic.* Internal cutaneous; *ms.* Musculo-spiral; *u* and *m.* Medio-ulnar; *g.* To the muscles in the neighbourhood.

Fig. 3. The distribution of the musculo-spiral and circumflex nerves on the dorsum of the flipper. (*s*) Dorsal surface of scapula; (*h*) Of humerus; (*r*) Of radius; (*u*) Of ulna; (*a*) Teres major muscle; (*b*) Triceps; (*c*) Circumflex appearing through the quadrilateral space; (*d*) Its branches to the deltoid; (*cs.*) To the skin of the shoulder; (*m*) Musculo-spiral appearing through the triangular space, and giving a branch to the triceps, and then spreading out in branches over the lower end of the humerus, and the ulna.

Fig. 4. Diagram of the Lumbo-caudal nerves. (*g*) Transverse processes of the vertebræ; (*k*) Chevron bones; (*c*) Spinal nerves; (*a*) Internal branches of the superior divisions; (*b*) Reinforcing twigs to these from the superior division next in order; (*e*) External branches of the superior divisions; (*N*) Superior longitudinal cord; (*d* and *f*) Inferior divisions of the spinal nerves passing down between the transverse processes. (*P*) Twigs from the sympathetic. Nos. 1 to 11 indicate the eleven nerves which correspond to the lumbar and sacral nerves in man; (*M*) Internal pudic or genital nerve; (*O*) Inferior longitudinal cord; (*R*) Nerves to the tail.

The Explanation of the wood-cuts, figures 5, 6, 7, is given in the Text.

The above illustrations are taken from drawings executed by Dr J. H. Scott, Demonstrator of Anatomy in the University of Edinburgh, and I am deeply indebted to him for the care he bestowed upon them.

NOTES OF A CASE OF DOUBLE AORTIC ARCH. By M. WATSON, M.D., *Professor of Anatomy, The Owens College, Manchester*. (Plate VIII.)

CASES in which there is persistence throughout life of both the vascular arches by the union of which the aorta is formed during intra-uterine existence are sufficiently uncommon to justify the publication of one which I had an opportunity of examining during last winter session. The case presents moreover some points of interest which do not appear to have been observed in those which, most closely resembling it, have been previously described.

This unusual arrangement of parts occurred in the body of a female between seventy and eighty years of age which had been sent to the anatomical room of the College for purposes of dissection. On opening the chest the trunk of the ascending thoracic aorta, instead of passing upwards and to the right, was observed to ascend exactly in the middle line, lying parallel to and directly in front of the trachea for a distance of three inches, and then to subdivide into two branches of unequal size. This trunk, which formed the ascending portion of the double arch, to be presently described, was situated entirely within the sac of the pericardium. *In front* of its origin from the base of the heart was the trunk of the pulmonary artery which almost at once passed to its left side, whilst *behind* it was the right branch of the same vessel, together with the left innominate vein, which, crossing from left to right to unite with its fellow, intervened between the ascending aorta and the trachea. On its *right* side were the right innominate vein and superior vena cava, and on its *left* the bifurcation of the pulmonary artery. Of the two branches into which this trunk divided, one, the calibre of which was about four times that of the other, passed backwards lying to the *right* of the trachea and œsophagus, arched over the right bronchus, and gained the middle line of the dorsal vertebræ, where it became continuous with the descending thoracic aorta. This branch along with the ascending aorta thus formed a true right aortic arch, the relations of which as respects its transverse portion were the following. It passed almost transversely backwards, extending from the trachea in front to the middle line of the anterior surface of the body of the fourth dorsal vertebra behind, and was crossed on its *outer* side from before backwards by the right pneumogastric nerve, the

right innominate vein, and close to its termination by the vena azygos major, which turned forward at this point to open into the superior vena cava. Its terminal portion was moreover invested by the right pleural membrane. To its *inner* side were the trachea, œsophagus, and right recurrent laryngeal nerve, the last of which ascended in the internal between the two tubes. In the *concavity* of the arch were situated the commencement of the superior vena cava and the right recurrent nerve, whilst from its *convexity* the following branches were given off from before backward. 1. The *Right common carotid* which was given off half an inch from the bifurcation of the ascending aorta, and passed obliquely upward and backward to gain its usual position in front of the cervical portion of the vertebral column. 2. The *right vertebral* artery which, separated at its origin by half an inch from the carotid artery, passed upwards and backwards, lying parallel to and behind that vessel as high as the fourth cervical vertebra, into the foramen transversarium of which it entered. 3. The *Right Subclavian*, which, arising from the highest point of the arch, and being closely applied at its origin to that of the right vertebral artery, arched upwards and outwards to gain the upper surface of the first rib over which it passed. On reaching the neck it gave off from its *first* part the internal mammary and inferior thyroid arteries, and from its *second* the superior intercostal and deep cervical branches. The transverse cervical and supra scapular arteries had been in all probability given off from its *third* portion; but this I could not determine by reason of the latter part of the artery having been removed previous to my examination of the dissection.

Passing now to the examination of the *left* aortic arch, it was seen to be composed of two parts, an *anterior pervious* represented by the smaller of the two trunks into which the ascending aorta divided, and a *posterior impervious*, represented by a thick fibrous band continuous in front with the arterial portion of the arch and attached posteriorly to the commencement of the descending thoracic aorta. These two parts thus completed an aortic arch lying to the *left* of the trachea and œsophagus, which corresponded exactly to the arch of the opposite side already described, as may be clearly seen by considering its relations. On its *outer* side the arterial portion of the arch was crossed from before backwards by the left innominate vein and left pneumogastric nerve, whilst the terminal impervious portion, measuring five-eighths of an inch in length, and three-eighths in breadth, was invested by the left pleural membrane. To the *inner* side of the arch were the trachea and œsophagus, the former lying in relation to its pervious, the latter to its inpervious portion, whilst the left recurrent nerve ascended in the internal between them. In the *concavity* of the arch was situated the ductus arteriosus, represented by a stout fibrous cord attached below immediately to the left of the bifurcation of the trunk of the pulmonary artery and blending above with the commencement of the impervious portion of left aortic arch. The recurrent nerve

hooked round the arch lying to the outer side and in contact with the ductus arteriosus. From the *convexity* of the arch the following branches were given off from before backwards. 1. The *Left Common Carotid*, which arose half an inch from the bifurcation of the ascending aorta, and passed upwards and backwards to gain its usual position at the root of the neck. 2. A very small artery which exactly corresponded in its place of origin to that of the vertebral artery from the arch of the opposite side. It passed obliquely upwards and backwards, and followed a precisely similar course to that of the right vertebral, lying behind and parallel to the left common carotid. It was pervious for only half an inch from its origin and degenerated into a delicate fibrous cord which, upon careful dissection, could be traced upwards lying upon the prevertebral fascia covering the longus colli and rectus major muscles as high as the 4th cervical vertebra, where it again became pervious, and entering the foramen transversarium of the 3rd cervical vertebra, terminated by joining the trunk of the left vertebral artery, to be presently described. 3. The *left subclavian artery*, which arched upwards and outwards to gain the upper surface of the first rib, over which it passed. From the first part of this artery in the neck were given off as distinct branches from its anterior aspect, the internal mammary, the inferior thyroid, and transversalis colli arteries, whilst from its posterior aspect the left vertebral artery took its rise. The latter branch, normal in respect to size, entered the foramen transversarium of the 6th cervical vertebra, beyond which its course and relations presented nothing remarkable.

The *descending thoracic aorta* formed by the union of the right and left aortic arches in front of the body of the fourth dorsal vertebra, passed downwards lying directly in front of the vertebral column, as low as the ninth dorsal vertebra, where it passed to the left of the middle line and disappeared from the chest by passing through the diaphragm.

From what has been said it will be observed that the right and left aortic arches were almost symmetrical, and together formed an arterial collar (obliterated certainly to some extent on the left side), including the trachea and œsophagus. The only deviation from complete symmetry consisted in the altered relations of the pneumogastric nerve and innominate vein of opposite sides, but this is sufficiently accounted for by the oblique course of the left innominate vein in order to unite with that of the opposite side to the right of the middle line. The pulmonary artery was normal, its left branch being connected, as already described, with the impervious portion of the left aortic arch by means of the ductus arteriosus. The right innominate vein followed the usual course, and crossed the right aortic arch from above downwards. The left innominate vein, formed in the usual manner, crossed the left aortic arch from above downward, but instead of passing from left to right on a plane *anterior* to that of the ascending aorta, it crossed *behind* that trunk so as to intervene between the aorta and the trachea. The superior

vena cava, by reason of this unusual course of the left innominate vein, was extremely short, but otherwise normal. The vena azygos major opened into the junction of the right and left innominate veins. The remaining veins of the thorax were normal.

The thoracic duct after entering the thorax maintained its usual relation to the aorta and vena azygos major as high as the termination of the latter, behind which, as well as the right aortic arch, it then passed. At the root of the neck it lay behind the first part of the right subclavian artery, and arching forwards, opened into the junction of the *right* subclavian and jugular veins. The duct, therefore, was *not* included within the aortic collar. Each pneumogastric nerve crossed the corresponding aortic arch, giving off its recurrent branch in the concavity of the same, that on the left side coming into relation with the ductus arteriosus, as already described. The phrenic nerve of each side passed *in front* of the corresponding subclavian vein at the root of the neck. With this exception their course was normal. There was no transposition of the viscera.

Comparing now the case just described with those which most closely resemble it, we find that cases of persistent double aortic arch have been reported by Malacarne[1], Hommel[2], Bertin[3], Siebold[4], Hyrtl[5], Zagorsky[6], Cruveilhier[7], Curnow[8], and Allen Thomson[9]. In all of these, with the exception of the last, both aortic arches were pervious throughout. In *it* a portion of the left aortic arch, as in the case just detailed, was obliterated, and formed a fibrous band, connected by one extremity to the subclavian artery, and by the other to the commencement of the descending thoracic aorta, thus forming, as Professor Thomson remarks, "a transition between the more common cases of right aortic arch without union to the left part of the aorta, and such cases as those of Hommel," and the other authors just mentioned, in which two aortic arches of nearly equal size closely encircled either the trachea alone or both trachea and œsophagus. In it, however, there was a considerable bulging or dilatation of the upper part of the descending aorta toward the left, to the point of which the impervious portion of the left aortic arch was attached, which is absent in my own case. And this is not without interest when viewed in connection with the development of the parts. As is well known, a complete double aortic arch presents a permanent condition of that early embryonic arrangement in which the fourth right and left vascular arches unite to form the descending thoracic aorta. Each of these arches consists of three portions,—an anterior, which forms the ascending or ventral aortic root; a transverse, formed by

[1] *Osservaz. in Chirurg.* 1788, II. 119.
[2] *Commercium literarium*, Norimb. 1737, p. 161.
[3] *Maladies du Cœur*, p. 433.
[4] *Journal für Geburtshülfe*, 1836. XVI.
[5] *Oesterr. medic. Jahrb.*, 1841. XXIV.
[6] *Mém. de l'Acad. des Sc. de St Pétersbourg*, 1824.
[7] *Cruveilhier*, 1867, p. 51.
[8] *Trans. Path. Soc.* Lond. 1875.
[9] Described in Prof. Turner's Memoir in *Brit. and For. Med. Ch. Rev.* 1862, p. 184.

the fourth visceral artery; and a posterior descending, or dorsal aortic root, composed of the dorsal anastomosing vessel, between the fourth and fifth visceral arteries, together with the continuation backward of the same vessel to unite with that of the opposite side, in the formation of the thoracic aorta. All of these portions on both sides remain pervious in cases of complete double aortic arch. In Prof. Thomson's case, again, the whole of these portions remained pervious on the right side, whilst on the left, the first and second, in addition to the upper and lower thirds of the third portion (these last being represented respectively by the artery above the ductus arteriosus, and the lateral bulging or dilatation of the descending thoracic aorta) remaining pervious, the rest of the arch was obliterated. In the case above related, however, the pouch-like dilatation of the descending aorta was wanting, the obliterated portion of the left arch being attached directly to that vessel. In it, therefore, we have an example of still greater obliteration of the left aortic arch than occurred in Prof. Thomson's case, the lower two-thirds of the dorsal aortic root having become impervious in the former, whilst only one-third of that root—the middle third—underwent complete obliteration in the latter. With regard to the relation of the thoracic duct to the arterial collar, both cases exactly correspond.

Turning now to the branches which are given off from the aortic arches, so far as one can judge from the comparatively few cases of double aortic arch which have been put on record, the most common arrangement appears to be, as indeed one would, on developmental grounds expect, that from each a carotid and subclavian artery is given off. The cases of Malacarne and Zagorsky, however, form exceptions to this rule. My own case appears to be the only one in which, in addition to the branches just named, a right and left vertebral artery was given off from the corresponding arch between the carotid and subclavian of the same side. That such is really the case there can be no doubt, as, although the left vertebral arising from the left arch was reduced to a mere fibrous cord in the greater part of its course, yet, having regard to its origin, relations, and termination, it was evidently homologous with the artery of the opposite side, the origin of each having been transferred from the subclavian artery of its own side to the corresponding aortic arch. The additional left vertebral artery arising from the left subclavian, corresponded as regards its origin, position, and relations, to the vertebral artery, as we usually see it; and inasmuch as the left side of the neck was thus supplied with *two* vertebral arteries, this case is to be grouped along with those, of which several have been reported, in which an accessory vertebral was present. In the cases in which this occurs on the left side, the usual arrangement is that one of the roots of the vertebral artery arises from the arch of the aorta, whilst the other is given off by the subclavian; and to this rule the present case forms no exception.

Lastly, with reference to the unusual position of the left innominate vein lying as it did *behind* the ascending aorta, the case presents a very unusual arrangement, as I have been unable to find any

account among the numerous recorded venous abnormalities, apart altogether from arterial irregularities, of such an occurrence. The explanation of its unusual position must, in the present state of our knowledge regarding the development of the large veins, be almost entirely hypothetical. Marshall[1] states that the transverse vein which in the fœtus unites the jugular veins of opposite sides at the lower part of the neck, and which ultimately forms the left innominate vein, is in the sheep formed by the junction of two small spur-shaped points, which project toward one another from the inner borders of the jugular trunks, immediately above the pericardium, on a level with the subdivision of the ascending aorta, and that these points ultimately coalescing, form the vein in question. The development of this transverse vein has not been studied in the human subject, but in all probability it resembles that of the corresponding vessel in the sheep. Now in the present case it is necessary to suppose that the above-mentioned spur-shaped projections, instead of uniting *in front* of the ascending aorta, extended inwards *behind* that trunk, and so gave rise to the anomalous position above described of the left innominate vein. That the plane of junction of these spur-shaped projections is not invariable, although *rarely* removed backwards, is proved not only by the present case, in which they appear to have united between the aorta and trachea, but also by two cases reported by Weese[2], in both of which they had united on a plane posterior to both trachea and œsophagus, the left innominate vein having been observed to cross from left to right behind both of these structures.

DESCRIPTION OF PLATE VIII.

R. C. A., L. C. A., Right and Left Common Carotid Arteries. R. V. A., L. V. A., Right and Left Vertebral Arteries. The accessory vertebral artery of the left side is not figured. R. S. A., L. S. A., Right and Left subclavian arteries. R. I. V., L. I. V., Right and Left innominate veins. R. S. V., L. S. V., Right and Left subclavian veins. I. J. V., Left internal jugular vein. D. A., Ductus arteriosus. R. Ph. N., Right phrenic nerve. R. P. N., L. P. N., Right and Left pneumogastric nerves. The hook in the right-hand figure indicates the œsophagus.

[1] *Phil. Trans.* 1850, (Part 1).
[2] *De ectopia cordis*, Berolini, Sect. 37, 48.

ON THE ACTION OF VANADIUM UPON THE INTRINSIC NERVOUS MECHANISM OF THE FROG'S HEART. By PROFESSOR ARTHUR GAMGEE, M.D., F.R.S., AND LEOPOLD LARMUTH, *Platt Physiological Scholar in Owens College.*

(*From the Physiological Laboratory of Owens College.*)

IN his memoir "On the Physiological Action of Vanadium," (*Philosophical Transactions*, 1875) J. Priestley recapitulates the facts which he has ascertained with reference to the action of this poisonous metal on the circulation in the following manner.

"A consideration of the experiments shews that the influence of vanadium upon the circulation is three-fold. In the first place, there is a diminution of blood-pressure, which, however, is not quite continuous, but is marked by intervals in which there is a tendency to regain the former height. Then alternate rises and falls take place with considerable regularity. In the second place, there is a disappearance of the respiration curves. And in the third place, there is irregularity and diminution of rapidity of the pulse, which, like the fall of the blood-pressure, is not quite regular. In the case of injection into veins there was scarcely time, owing to the rapidity of death, for the development of the marked fluctuations noticed when injection was hypodermic.

"The disappearance of respiration curves can only be due to some alteration of the vaso-motor centre, whose oscillations of activity are the cause of them. The marked fall of blood-pressure might be due to one, or more, of the following circumstances: 1, Paralysis of the vaso-motor centre; 2, peripheral irritation of depressor nerves; 3, relaxation of arterial tonus due to other causes than vaso-motor paralysis; 4, weakening of the heart's action. The alteration of the pulse may be

caused by 1, some action upon the vagi; 2, poisoning of intra-cardiac centres; 3, poisoning of muscular substance of heart; 4, diminution of blood-pressure. As previous division of the vagi does not seem in the least to alter the circulatory effects of poisoning by vanadium, it is clear that none of these effects can be attributed to the action on the vagi. It is, moreover, evident from experiments detailed elsewhere in this paper, that there is no poisoning of the muscular substance of the heart itself.

"Further, the fact that vanadium does not paralyse unstriped muscles in other regions of the body (as in the intestines) renders it probable that there is no direct action upon the muscular walls of the arteries. We may therefore at once eliminate both these possibilities from the question. It will be seen on comparison that the fluctuations in blood-pressure and in pulse are only sometimes coincident; neither will, therefore, serve as sufficient explanation of the other, although the effects may be partially due to their inter-action. There remains, therefore, the vaso-motor system of nerves, with the depressors, and the intra-cardiac nervous mechanism, to which we must look for the chief explanation of the phenomena under consideration.

"From the experiments in which the cord was divided in the neck, we gather that the effects of vanadium-poisoning upon the pulse occurred as usual, while the diminutions and fluctuations in blood-pressure were no longer visible, being indeed replaced by a rise. As in those experiments the vaso-motor centre, the accelerators and the vagus-centre terminations were eliminated (the vagus-terminations by means of the curari which was injected), we are driven to the conclusion that the depression and fluctuations of blood-pressure are for the most part due to some action of the poison on the vaso-motor centre; and that the irregularities of heart-beats are caused by an affection of intra-cardiac ganglia. The former conclusion is strongly confirmed by the disappearance of respiration-curves, which must be due to vaso-motor mischief, and by the fact that other centres in the cord are acted on by vanadium: hence it seemed hardly necessary to perform any special experiments after elimination of the depressors. The latter

conclusion is fully borne out by Experiment LIII., on a frog, where the usual diminution followed in a heart which was directly observed after the removal of all extra-cardiac nervous influences. The rise of blood-pressure which follows injection into the veins of rabbits, whose spinal cord has been cut, is considered to be due to the greater vigour of the heart, which was noticed."

Thoroughly satisfactory as were the investigations on the effects of vanadium in the circulatory system of warm-blooded animals, it appeared that additional experiments were desirable in order to investigate more closely the precise mode in which vanadium affects the intra-cardiac nerve-centres, and we therefore undertook an examination of the action of vanadium upon the frog's heart.

In Priestley's researches the compound of vanadium employed was invariably the sodium ortho-vanadate, Na_3VO_4, of which standard solutions containing exactly 5 per cent. of V_2O_5 were used. In the present research, for reasons which will appear in the sequel, the sodium salts of the ortho-, meta-, and pyro-vanadic acids were employed at various times, the solutions always being neutral, and containing a quantity of vanadium corresponding to 5 per cent. of V_2O_5.

The three compounds employed have the following formulæ:

1. Meta-vanadate of Sodium, $NaVO_3$.
2. Pyro-vanadate of Sodium, $Na_4V_2O_7$.
3. Ortho-vanadate of Sodium, Na_3VO_4.

The compounds of vanadium, and the standard solutions used throughout were prepared under the direction of Professor Roscoe, F.R.S., by Mr Taylor, Demonstrator of Metallurgy in Owens College.

In some of our experiments Rana esculenta was employed, but in the greater numbers Rana temporaria, in a few the large American Bull-frog.

Methods of investigation.

In some of our experiments the movements of the hearts of pithed frogs were observed, *in situ*, with the eye, and the

solution of which the poisonous action was being investigated was injected through the abdominal vein. In some few experiments the poisonous solution was applied to the external surface of the heart. In some cases, as in the experiments undertaken to ascertain the comparative poisonous activity of the three vanadic acids, the poison was introduced into the lymph-sacs of frogs, the heart being exposed and watched after the general paralytic phenomena which are induced by the compounds of vanadium had become developed. In the greater number of experiments a modification of the method used by Ludwig and Coates was employed, of which the essential feature consisted in the serum being kept in a state of circulation by means of the frog's heart, except during the time when tracings were being taken. The frog was supported on a horizontal plate, and its vena cava connected with a flexible tube leading to a reservoir of serum, the height of which could be accurately regulated. This reservoir consisted of a short test-tube, into the bottom of which a finer tube (for connection with the above-mentioned flexible tube) had been fused. Supported directly over the mouth of this test-tube was a thermometer, the bulb of which was immersed in the serum in the reservoir. The aorta was connected with a long glass tube attached to a gauge precisely similar to that used by Coates. The same limb of the gauge was connected with a long flexible tube terminating in a fine glass nozzle, which was carried round and fixed against the thermometer at a height of about 2 inches, or rather more, above the surface of the serum in such a manner that, as the serum was driven through the nozzle, it spread over the thermometer-stem in a thin film which flowed down to the reservoir, thus presenting a very large surface for aëration. When tracings were about to be taken, the tube from the proximal limb leading to the aërating nozzle was guarded by a clip, whereupon the blood-pressure raised the mercury in the distal limb, and movements were recorded.

The serum employed in the majority of the experiments was that of the rabbit. The capacity of the serum reservoir was 5 cub. cents.

EXP. I. (3 | 2 | 76.) A frog (R. esculenta) was pithed and the heart prepared for Coates's experiment. Reddish sheep's serum employed.

H. M.	
2 . 20.	Heart connected with serum-reservoir and gauge.
3 . 20.	Normal tracing taken. Heart beats vigorously, between 5 and 6 times per 10 seconds.
3 . 21.	Circulation of poisoned serum commenced. The serum was prepared by mixing 1 volume of standard solution of sodium ortho-vanadate (containing 5 per cent. of V_2O_5), with 50 volumes of sheep's serum.
3 . 24.	A tracing taken. Contractions of the heart are much slower, 1 in 3 seconds. The contractions are, however, perfect and regular.
3 . 30.	Another tracing taken. Contractions not as vigorous as before, but occur with the same frequency. The ventricle appears to be abnormally contracted at apex. A vermicular contraction of the ventricle occurs at intervals; this runs from base to apex, and pinches off, as it were, the ventricular apex. The auricles are contracting normally.
3 . 38.	Another tracing taken. No marked change.
3 . 55.	Vermicular contractions of ventricle very marked; the ventricle contracts sluggishly.
4 . 25.	Ventricles still contracting, though very inefficiently.
4 . 40.	Tracing taken; the rise of the mercury in the manometer at each systole is indicated in the tracing by slight waves in the line traced by the pen.

EXP. II. (4 | 2 | 76.)

12 . 15.	Rana esculenta decapitated, pithed, and heart prepared.
12 . 30.	Pure serum allowed to flow through the heart.
12 . 53.	Heart contracting vigorously, once in 2·75 seconds.
1 . 48.	Normal tracing taken. Contractions slower, but vigorous, 1 in 5 seconds.
2 . 5.	Another tracing taken. Agrees with the preceding. Serum poisoned with solution of Na_3VO_4 (1 volume of standard solution of the poison to 50 of sheep's serum) allowed to circulate through the heart.
2 . 10.	Contraction of heart slower, though more vigorous than before.
2 . 15.	Peristaltic contraction of ventricle, the systole of which is becoming more sluggish.
2 . 30.	Contraction of ventricle very slow and imperfect, so that a satisfactory tracing cannot be obtained.
2 . 45.	Auricles are contracting slowly, ventricle is in a state of permanent contraction; occasional vermicular contractions of ventricle.

3 . 0. Ventricle is contracting peristaltically, once in 30 seconds; auricle contracting once in 10 seconds.
3 . 15. Occasional slight vermicular contractions of ventricle, about once in 45 seconds; auricle contracts once in 15 seconds.
4 . 0. Auricles still contracting feebly; only very occasional slight vermicular contractions of ventricle.

Exp. III. Rana temporaria. Circulation of rabbit's serum, at T. 14° C, through heart.

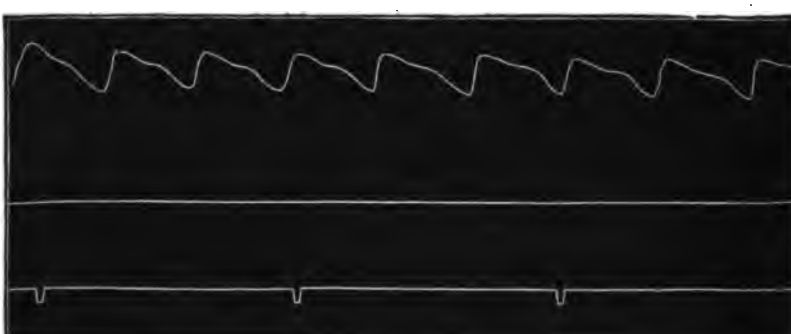
H. M.
2 . 40. Frog prepared.
3 . 0. Aorta has been connected with the manometer, heart has been washed out with reddish rabbit serum, and is contracting fully and vigorously.
4 . 0. Poisoned serum allowed to circulate. As it reached the heart the organ commenced to beat a little more rapidly.
4 . 5. Heart contracting once in 2 seconds.
4 . 10. Vermicular contractions of ventricle. One contraction of ventricle to 3 of auricles.
4 . 15. Tracing indicates that the heart is contracting 1 in 2·2 seconds, much less vigorously than before.
4 . 30. Contractions more prolonged and feeble.
4 . 40. Auricles contracting once in 7 seconds; ventricle feebly, once in 20 seconds.

(Experiment not continued).

Exp. IV. (8 | 2 | 76.) Rana temporaria. Rabbit's serum at T. 16° allowed to circulate.

1 . 0. Frog prepared.
1 . 20. All connections have been made. Heart has been washed out with rabbit's serum; is beating vigorously.
1 . 45. Normal tracing taken. Heart beats fully 6 times in 10 seconds.

Fig. 1.



2 . 0. Another tracing, exactly similar to the preceding, taken.

2 . 15. Circulation of poisoned serum commenced (1 volume of standard solution of Na_3VO_4 to 50 of serum).

2 . 20. The characters of the contractions, and therefore of the tracings, have altered considerably; they have become much less frequent, the force of the contraction has diminished, whilst the length of the systole has increased in a marked manner (Fig. 2).

Fig. 2.

2 . 40. Tracings taken since the last shew exactly the same characters; the ventricle is nearly always in a state of systole, the diastolic intervals being very short.

3 . 0. Since the last note the heart appears to have commenced to recover from the effects of the poison, the contractions of the ventricle becoming more complete and more rapid.

3 . 40. Heart appears to have recovered completely, contracting four times in 10 seconds.

3 . 45. A fresh quantity of the standard solution of Na_3VO_4 added to the serum in the reservoir. The mixture then consisted of 2 volumes of solution of the poison to 50 volumes of serum.

3 . 47. The ventricle is in a state of strong and persistent contraction. The auricles contract slowly.

3 . 50. It has been impossible to obtain any tracing since the poisoning. Auricles slowly pulsating.

4 . 0. Ventricle now at rest in diastole; some portions of the ventricles are, as it were, pinched off by local contractions. Auricle and sinus venosus contracting sluggishly.

EXP. V. (11 | 2 | 76.) Rana temporaria. Rabbit's serum at a temperature of 15° C allowed to circulate through heart.

2 . 45. Frog decapitated and prepared for experiment.

3 . 0. Connections have been made, and heart washed out with serum.

3 . 15. Normal tracing taken (Fig. 3).

3 . 42. Heart has been beating with perfect regularity, and a tracing taken now is exactly similar to that taken at 3.15. Poisoned serum (1 volume of Na_3VO_4 solution to 50 of rabbits' serum) allowed to circulate.

Fig. 3.

3 . 44. Ventricle is in a state of strong and persistent contraction; auricles contracting rhythmically.

3 . 47. A tracing taken; the elevations are due to the auricular contractions, as the ventricle is not beating (Fig. 4).

Fig. 4.

3 . 49. After a short time the ventricle has commenced to contract again vigorously; contractions recur rhythmically for 5 minutes, then cease, the ventricle remaining in a state of systole.

4 . 0. Ventricle at rest in a state of contraction. Auricles contracting normally.

4 . 5. By raising the pressure of serum in the heart, the ventricle commences to contract. The contraction runs from base to near apex, but stops short so as to pinch off, as it were, a portion of the apex. Upon diminishing the pressure the ventricle ceases to contract in systole.

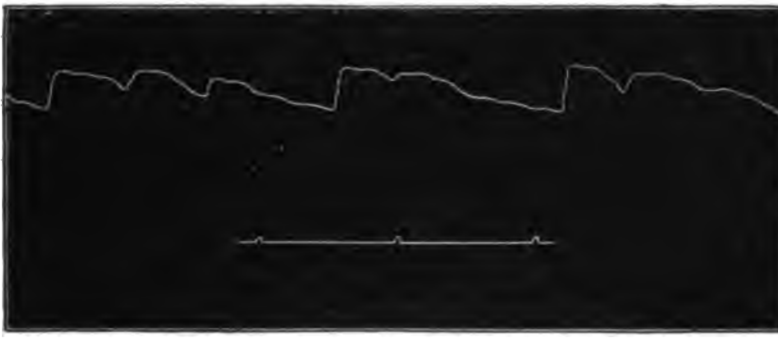
4 . 15. The ventricle contracts only occasionally, whilst the auricles contract with regularity.

4 . 17. The condition of the heart is well shewn by the annexed tracing (Fig. 5). Contractions of the ventricle succeed each other slowly, in groups of two or three, and then a prolonged diastole follows.

4 . 55. The heart is recovering somewhat from the effects of its first poisonous dose.

5 . 10. Although there are still evidences of the action of vanadium upon the heart, it is determined to increase the strength of the poison.

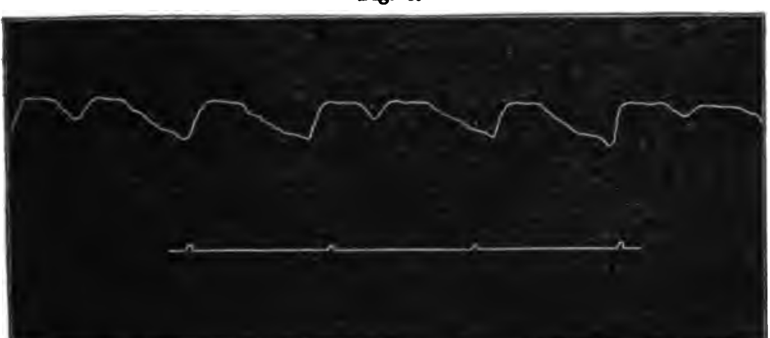
Fig. 5.



5 . 15. One more volume of the solution of $Na_3 VO_4$ added to the serum.

5 . 16. After two contractions of the ventricle a pretty long pause occurs; then generally a single slow contraction; followed again by two contractions, thus:

Fig. 6.



5 . 20. Ventricle in a persistent semi-contracted state; *i. e.* diastole never complete.

Observations discontinued.

Remarks.—The five experiments which have preceded illustrate the influence exerted by a *small* dose of vanadium when mixed with serum, and allowed to circulate through the separate frog's heart. In them, as has been mentioned in the notes of the individual experiments, one volume of a weak solution of sodium ortho-vanadate was mixed with 50 volumes of reddish rabbit's serum; as the solution of vanadate contained a quantity of vanadium corresponding to 5 per cent. of $V_2 O_5$, the percentage of the poisonous metal contained in the poisoned serum was ·098. In the experiments which follow the effect of a dose twice as large are shewn.

Exp. VI. (15 | 2 | 76.) Rana temporaria.

H. M. Rabbit's serum at T. 18° C. employed.

2 . 0. Frog decapitated and heart prepared for the experiment.
2 . 45. Normal tracing taken; heart is beating vigorously.
3 . 0. Circulation of poisoned serum commenced. (1 volume of standard solution of Na_3 VO_4 mixed with 25 volumes of serum.)
3 . 3. Ventricle contracting very slightly at long intervals.
3 . 5. Apex of ventricle firmly pinched off; the rest of the ventricle in a state of distension; auricles contracting slowly.
3 . 25. Ventricle is firmly contracted; auricles are contracting slightly and sluggishly.
4 . 20. Ventricle as before. Auricles are contracting about once every 20 seconds.

No tracings could be obtained after the poisoning; the normals have therefore not been copied.

Exp. VII. (15 | 2 | 76.) Rana temporaria.

Rabbit's serum at T. 18° employed.

4 . 20. Frog's heart prepared; pure serum allowed to circulate.
4 . 30. Normal tracing taken. Heart is beating vigorously and regularly.
4 . 45. Another tracing taken; allowed poisoned serum (1 : 25) to flow through.
4 . 47. Ventricle beating feebly; does not relax completely during diastole; auricles are contracting quite normally.
4 . 50. Ventricle strongly contracted; auricles beating feebly.
5 . 5. Auricular contractions continue, though feeble.
5 . 30. Ventricle still contracted; auricles still beating.

In this experiment it was again impossible to obtain any tracings after the poisoning.

Exp. VIII. (21 | 2 | 76.) Rana temporaria.

H. M. Rabbit's serum used. Temperature not known.

3 . 20. Frog's heart has been prepared and washed out with rabbit's serum.
3 . 30. Normal tracing taken.
3 . 45. Poisoned serum allowed to circulate (1 of standard solution of Na_3 VO_4 to 25 of serum).
3 . 46. Ventricle contracting vigorously.
3 . 46.5. Ventricle in a state of complete and continuous contraction; auricles beating slowly.
3 . 50. Heart in same state as before, auricles beating slowly.
4 . 30. Heart in a state of distension; neither auricles nor ventricles beating; upon pinching, slight contraction of the ventricle is produced.

EXP. IX. (18 | 2 | 76.) Rabbit's serum. T. 19°.

3 . 35. Heart of rana temporaria has been prepared and rabbit's serum allowed to circulate. Heart beats normally.
3 . 45. Normal tracing taken.
3 . 50. Poisoned serum allowed to flow through heart (1 of standard solution of Na_3VO_4 to 24 of serum).
3 . 52. Ventricle firmly contracted. Auricles beating normally.
4 . 30. Condition of heart exactly the same as before.
4 . 50. Ventricle less relaxed than before; auricles beating as at first.
5 . 0. Ventricle fully distended and at rest. When pinched it makes a single sluggish contraction; auricles contract normally.
6 . 0. Ventricle distended; a local contraction of ventricle follows pinching: auricles contracting normally.

EXP. X. (21 | 2 | 76.) Rana temporaria.

3 . 20. The frog having been decapitated and pithed, heart prepared and connected with Coates' apparatus. Pure rabbit's serum allowed to circulate at first.
3 . 30 and 3 . 40. Perfectly normal tracings taken. Heart beating regularly and vigorously.
3 . 45. One volume of standard solution of Na_3VO_4 mixed with 25 volumes of the serum.
3 . 46. Very vigorous contraction of ventricle.
3 . 46.5. Ventricle in a state of complete and persistent systole.
3 . 50. Heart in same state as before; auricles beating slowly.
4 . 50. Heart in a state of distension; neither auricles nor ventricles are beating. Upon pinching the ventricle slight contractions follow.

The ten experiments which have preceded illustrate in a very satisfactory manner the phenomena which are observed when serum poisoned with a soluble vanadate circulates through the excised heart of the frog.

When the serum contained the poison in the proportion of 0·098 per cent. of V_2O_5 it was observed that the force of the ventricular systole was very much diminished, that the ventricle passed into a state of persistent contraction for a time, or, in many cases, that whilst portions of the ventricle were in a state of diastole others were firmly contracted. Generally, however, such a proportion of the poison did not kill the heart, and the effects which were at first produced appeared gradually to be recovered from. On then increasing the quantity of poison in

the circulating serum the ventricle was usually, but not always, brought to a complete standstill in a state of firm contraction.

When the amount of the poison contained in the serum is about twice as large, viz. amounts to 0·192 per cent., the effects produced follow much more rapidly. Usually within one or two minutes the ventricle stops in a state of rigid contraction, whilst the auricles continue their rhythmical movements, enfeebled however, for a considerable length of time.

The reader will not fail to perceive that the phenomena which have yet been described are in essential particulars the same as occur in poisoning by digitalis. Like digitalis, vanadium seems to cause a slowing of the heart by abridging the diastolic period, *i.e.* by lengthening the systole, and to bring the ventricle to a standstill in systole. It is to be observed that not unfrequently the heart which has been poisoned by vanadium and the ventricle of which has been for a considerable time in a state of rigid contraction, becomes completely relaxed.

In the closer study of the action of vanadium on the frog's heart there were two sets of experiments which appeared likely to prove of special interest: the first consisting in observing the effects of excitation of the vagi on the poisoned heart; the second in ascertaining whether atropia modified in a special manner the action of the drug.

EXP. XI.

H. M.	
12 . 20.	Large Canadian bull-frog pithed and prepared for Coates's method. Vagus exposed and ligature passed beneath it. Reddish rabbit serum used in the experiment. After the left aorta had been connected with the gauge, platinum electrodes connected with the secondary coil of Du Bois Reymond's apparatus were placed under the right vagus. With the secondary coil at 40 Cm there was slight slowing; at 30 Cm the effect was greater, but the heart did not stop; at 20 Cm the heart stopped at once.
12 . 45.	A normal tracing taken. The temperature of the serum circulating is 20·5° C.
12 . 54.	The pure serum replaced by serum mixed with $\frac{1}{25}$th of its volume of standard solution of $Na_4V_2O_7$.
12 . 55.	Ventricle observed to be abnormally contracted; auricles beating normally.
12 . 56.	Ventricle completely and firmly contracted; at intervals

complete dilatation of circumscribed portions, the apex, for instance, being at times completely dilated and pinched off.

12 . 57. Ventricle still strongly contracted. Vagus excited; secondary coil at 20 Cm. Auricles cease pulsating but ventricle remains *firmly* contracted.

1 . 0. Right vagus again excited; complete stoppage of auricle, but no relaxation of ventricle.

1 . 1. Auricles alone pulsating; at intervals complete local dilatations of ventricle take place.

1 . 5. Heart still in same condition as before.

1 . 10. Ventricle completely and persistently contracted; auricles pulsating slowly but otherwise normally. Vagus irritated; auricles stop but ventricle is not affected.

1 . 13. Auricles are beating 9 times in 30 sec.; ventricle still contracted.

1 . 20. Auricles contracting 6 times in 30 sec.; ventricle contracted as before.

1 . 25. Ventricle firmly and completely contracted; small portions still dilated as before; auricles beating slowly but regularly. On exciting the vagus auricles stop but ventricle does not relax. During excitation the local dilatations of ventricle do not occur at all, the whole ventricle being firmly contracted.

1 . 31. To the poisoned circulating serum one drop of a ·5 p.c. solution of atropin sulphate was added.

1 . 35. On exciting the vagus no stoppage of the auricles takes place; ventricle still contracted though the local dilatations are somewhat larger.

1 . 40. Vagus excited; secondary coil full up to primary. No stoppage of the auricles. Ventricle firmly contracted.

1 . 45. Auricles beating 8 times in 30 seconds. No stoppage on exciting vagus; secondary coil at 0 Cm.

1 . 50. Ventricle becoming partially distended and not pulsating. Auricles contracting 5 times in 30 seconds. No stoppage on exciting the vagus.

2 . 0. Ventricle further dilated; not pulsating; mechanical and electrical stimulation produce no contractions; auricles still pulsate feebly and not arrested by powerful excitation of the vagus.

This was the only experiment in which excitation of the vagus was practised after poisoning by vanadium; the results which it yielded were, however, so positive that it appeared useless to repeat it.

This experiment proves, most conclusively, that after contraction of the ventricle of the frog's heart has been induced by vanadium, relaxation of the heart cannot be induced by exciting the vagus. It however teaches us that this is not due to any paralysis of the trunk of the vagus nor of its terminations, for

when excited it was able efficiently to inhibit the auricular movements, until atropia acted upon the heart, when the inhibitory mechanism was readily paralyzed, without any modification in the effects of vanadium upon the heart being induced.

In two sets of experiments, which for the sake of brevity are not quoted, the influence of atropia in modifying the action of vanadium was examined. The same quantity of a standard solution of sodium pyro-vanadate was injected into the abdominal vein of two frogs, one of which had been atropized. In both sets of experiments the result was exactly the same.

In another experiment the heart was prepared for Coates' method, and rabbit's serum poisoned with atropia was allowed to circulate through it. After obtaining a normal tracing the serum was poisoned with solution of sodium pyro-vanadate (1 volume of standard solution to 26 of serum), when the normal effect of vanadium was induced, viz. stoppage of the ventricular movement in systole.

In commencing the discussion of the mode in which the changes which have been described are brought about, it appears natural to enquire whether they are due to an action of vanadium upon the muscular substance of the heart or upon its intrinsic nervous mechanism, or upon both.

In the case of digitalin, veratria, and even antiar, it has been advanced that the state of rigid contraction of the ventricle which is induced by these drugs and which usually passes directly into rigor, is due to an action which they exert upon the protoplasmic substance of the heart, for these poisons are known to affect voluntary muscle, and therefore an action upon the muscular tissue of the heart is intelligible. Even these drugs cannot be considered to exert their action upon the heart merely by affecting its muscular structure, for whilst their ultimate effect on the ventricle is nearly the same, there appear to be in each case distinctive phenomena which can only be explained by supposing that they affect in different manners or more or less profoundly the nervous structures which are associated with the contractile elements. That their action is one which at first affects nervous rather than contractile elements, appears indeed obvious from the fact that all these poisons bring the ventricle to a standstill long before they affect the

auricle; in the case of antiar the auricle actually beats more powerfully after the action of the poison than before[1]. Now a poison which acted primarily upon the muscular structure of the heart would presumedly exert its action more readily upon the thin-walled auricles than upon the more fleshy ventricle. It is, however, without doubt a most difficult task, in these cases, to unravel the muscular and nervous effects so as to be able with anything like precision to discover how great a share is to be attributed to an impairment of the properties of the muscular tissue, and how much is due to an alteration in the action of the nervous mechanism proper.

In the case of vanadium the researches of Priestley prove very conclusively that whilst acting injuriously upon and ultimately killing voluntary or involuntary muscles immersed in solutions of its compounds, vanadium is not properly a muscular poison, *i.e.* after death has been induced by a compound of vanadium the contractility of muscle is found to be unaffected, and the amount of work done by such muscles does not differ from that done by the same muscles of other frogs not killed by vanadium[2]. Upon which of these two sets of facts shall we rely in interpreting the phenomena induced in the heart when it is fed with serum poisoned by vanadium? The majority of persons will probably say that the first referred to, which prove that a solution of vanadium when acting directly upon a muscular structure affects its irritability, are most conclusive, and that we should, *à priori*, expect that when investigated by the method of Ludwig and Coates an action of vanadium upon the heart would be discovered, and that a great part of that action would be referable to a poisoning of the contractile element.

Such indeed is our own opinion—vanadium, at any rate when present in quantity in the blood or serum circulating through the heart, doubtless acts as a poison of the contractile tissue of the organ; though this cannot, however, be considered to be its only action, for if it were, how could we explain the

[1] Some effects of Upas Antiar on the Frog's Heart, by M. Foster, M.D., F.R.S., *Journal of Anatomy and Physiology*, Vol. x.

[2] A muscular poison may be defined as one which, in exerting its toxic action, *necessarily* impairs muscular contractility; this impairment is best measured by ascertaining, first, the duration and character of contraction, and secondly, the power of doing work. A. G.

continued action of the auricles long after the ventricle has been arrested?

It has been shewn that vanadium induces a permanently contracted condition of the ventricle, which ceases to beat, whilst the auricles pulsate more slowly than normally, but yet with regularity. This contracted condition of the ventricle differs from that induced by digitalis in two important particulars: firstly, it does not usually pass into rigor mortis, the heart becoming frequently dilated when it dies; secondly, the contracted condition of the ventricle is not affected by irritation of the vagus, though this nerve retains its power of inhibiting the auricles.

In poisoning by vanadium it is obvious that there is no affection of the terminations of inhibitory nerves in the heart, and no affection of the inhibitory nerve-centres which have been surmised to exist; there is, certainly, no paralysis of inhibitory nerve-centres connected with the auricles, and it would be surely pushing ingenuity to a dangerous extent to speculate upon the existence of a special set of inhibitory centres for the ventricular portions of the heart, which are paralyzed by vanadium and which are quite independent of other inhibitory centres for the auricle, over which vanadium has no action! If there were better grounds for the hypothesis of the existence of inhibitory centres in the heart than the fact that the action of one or two interesting cardiac poisons cannot be in any way explained without introducing such centres into our scheme of cardiac innervation, we might as an alternative speculation to the first advance a second—that possibly vanadium impairs the conductivity of the nerve-fibres which bring into communication the inhibitory and motor ganglia of the ventricular portion of the heart; but to speculate in this way appears to us quite puerile.

ON THE POISONOUS ACTIVITY OF VANADIUM IN ORTHO-, META-, AND PYRO-VANADIC ACIDS.

By LEOPOLD LARMUTH, *Platt Physiological Scholar, Owens College.*

(*From the Physiological Laboratory of Owens College.*)

CERTAIN observations which were made in the Laboratory of Owens College at the time when Priestley was investigating the physiological action of vanadium, led that observer and Dr Gamgee to think it possible that the poisonous activity of vanadium might differ in different nearly related compounds —that, probably, the same amount of vanadium would possess a greater poisonous intensity if existing as a pyro-vanadate, or meta-vanadate, than as an ortho-vanadate. To test the accuracy of this surmise, I made, at the request of Dr Gamgee, some experiments which, though few in number, appeared to point decidedly to the conclusion that a given quantity of vanadium is more poisonous as sodium pyro-vanadate, than sodium meta-vanadate, and still more so than as ortho-vanadate. The experiments would probably be too few to entitle one to draw important conclusions from them, had they not been confirmed by the much more extended research on the sodium salts of the exactly corresponding phosphoric acids—a research which has demonstrated that, whilst ortho-phosphates are inert bodies, meta- and pyro-phosphates, and especially the latter, are possessed of considerable activity. I quote from my note-book four sets of experiments which clearly shew that in the case of frogs, ortho-vanadic acid is a less poisonous substance than meta- and pyro-vanadic acids, and in the case of rats, ortho- is less poisonous than pyro-vanadic acid.

In these experiments three standard solutions were employed, prepared by Mr Taylor, Demonstrator in Metallurgy in Owens College, under the superintendence of Professor Roscoe, viz.:

1. A solution of Pyro-vanadate of Sodium,

$$Na_4V_2O_7.$$

2. A solution of Meta-vanadate of Sodium, $NaVO_3$.

3. A solution of Ortho-vanadate of Sodium, Na_3VO_4.

These solutions all contained 5 p.c. of V_2O_5. In addition we were supplied with some solid ortho-vanadate of sodium, to be weighed out and dissolved immediately before being used; the ortho-vanadate is sufficiently unstable to render it advisable that this should be done in some experiments.

EXPERIMENTS I. II. and III. Three frogs designated α, β and γ were accurately weighed, and then 1 cubic centimetre of solutions of the three sodium vanadates were injected under the skin.

α (META-VANADATE).
RANA TEMPORARIA.
Weight 33·57 grms.
1 cc. of Standard Solution of Na VO_3 injected.

In 4 minutes mouth gapes widely and frog makes extraordinary movements as if of retching.

In 10 minutes extends hind legs convulsively.

23 minutes. Lower jaw is drooping. Otherwise appears normal.

55 m. Much as before. Lower jaw still drooping. Movements sluggish and uncertain.

60 m. Lies extended.

65 m. When legs dipped in dilute acid, no reflex movements are induced.

95 m. Upon exposing heart it is found to have stopped beating. On exciting the ventricle mechanically a contraction occurs.

100 m. Heart begins to beat frequently with moderate vigour.

110 m. Heart beating languidly.

125 m. Heart has ceased to beat. On pinching it no contraction.

β (PYRO-VANADATE).
RANA TEMPORARIA.
Weight 31·21 grms.
1 cc. of Solution of $Na_4V_2O_7$ injected.

Immediately after injection appears much excited, leaping about under the bell-jar.

In 9 minutes floor of mouth seems to be bellied downwards.

14 m. Quiet; moves when touched; executes spontaneous movements.

22 m. Sprawls; leaps sprawlingly.

23 m. Lower jaw droops, *i.e.* mouth gapes. Clonic spasms of both hinder extremities.

24 m. Complete paralysis.

28 m. Reflex action abolished.

33 m. Heart exposed, contraction of auricles only; ventricle distended with blood.

38 m. Heart contracts.

43 m. Heart greatly distended.

73 m. Very feeble and irregular beats of heart.

γ (ORTHO-VANADATE).
RANA TEMPORARIA.
Weight 22·26 grms.
1 cc. of Solution of Na_3VO_4 injected.

27 minutes after. Frog seems not perceptibly affected.

70 m. Still quite normal.

130 m. Appears sluggish.

145 m. Sprawling. Leg not drawn up when pinched. When dipped in same dilute H_2SO_4 as α and β vigorous reflex movements.

160 m. Reflex action diminished but not abolished.

170 m. Legs no longer drawn out of acid. Heart exposed; found gorged with blood and beating slowly and irregularly.

EXPERIMENTS IV. V. and VI. Again three active, healthy, frogs were weighed and had injected under their skin quantities of the three salts corresponding in each case to the same quantity of V_2O_5 viz. ·05 grms.

α (META-VANADATE).

R. T. Weight 31·58 grms. 1 cc. of Standard Solution of $NaVO_3$.

In 18 minutes movements are sluggish. Jaw droops.

27 m. Lies quietly prone. Respirations have ceased. No paralysis of limbs.

36 m. Lower jaw droops. Incipient paralysis of limbs.

37 m. Slight spontaneous movements.

42 m. Cornea quite sensitive. Legs are drawn up sluggishly after being extended. Lies sprawling still.

106 m. after. Reflex action not abolished.

β (PYRO-VANADATE).

R. T. Weight 31·08 grms. 1 cc. of Standard Solution of $Na_4V_2O_7$.

20 minutes. Lies on belly; respiration has ceased. Jaw not drooping.

23 m. Moves in an imperfect, cramped manner.

27 m. Incipient paralysis of limbs.

34 m. Legs lie sprawling.

42 m. Reflex movements on pinching toes.

97 m. Completely paralyzed; no reflex movements on pinching.

182 m. When immersed in acid, legs sluggishly drawn out.

192 m. Heart exposed, auricles beating slowly; ventricle tightly contracted.

γ (ORTHO-VANADATE).

R. T. Weight 31·94 grms. 1 cc. Solution of Na_3VO_4 (Recently made).

26 minutes. Perfectly normal.

56 m. Perfectly normal.

71 m. Somewhat sluggish.

96 m. Lower jaw droops, leaps when touched.

127 m. Moves sprawlingly and falls on its back.

176 m. When feet dipped in acid, not withdrawn.

206 m. Heart still beating, though very feebly.

EXPERIMENTS VII. and VIII. Two white rats of as nearly as possible the same weight were chosen; under the skin of one was injected a recently-prepared solution of ortho-vanadate; under that of the other a solution of pyro-vanadate containing an equivalent quantity of V_2O_5.

RAT α.

Ortho-vanadate of Sodium.
Weight of Rat 208 grammes.

March 21, 1876.

3 h. 5 m. P.M. Injected 0·5 cc. of a solution of ortho-vanadate containing V equal to 0·025 of V_2O_5 injected under the skin.

3.10. Seems perfectly normal.

3.25. Still quite unaffected.

4.50. Perfectly normal. Is moving about actively.

March 22.

11 A.M. Appears rather sluggish; otherwise normal. Eats and drinks. Has no diarrhœa.

2.10. Animal now suffering from diarrhœa. Fæces very fluid and contain much mucus.

March 23.

Found dead this morning.

RAT β.

Pyro-vanadate of Sodium.
Weight of Rat 220 grammes.

March 21, 1876.

3 h. 11 m. P.M. Injected 0·5 cc. of standard solution of $Na_4V_2O_7$, containing V equal to 0·025 of V_2O_5.

3.20. Very quiet. Disinclined to move. Respiration gasping.

3.45. Seems drowsy, moving sluggishly.

3.50. Lies on the side or on the belly, with legs outstretched.

4.15. Still lying on side; is drowsy but moves when touched. Has diarrhœa. Pulpy fæces mixed with mucus.

4.30. When touched, moves about unsteadily and uneasily.

March 22.

In the morning found very sluggish. Great lachrymation. Respirations very laboured.

At 3.15 was found dead.

EXPERIMENTS IX. and X. Again two white rats experimented upon. Plan of experiments same as before; the dose of vanadium increased.

RAT α.
Ortho-vanadate of Sodium.
March 23, 1876.
Weight of Rat 158 grammes.

At 12 h. 45 m. P.M. Injected 0·1 grm. of Na_3VO_4 dissolved in 1 cc. of water (=0·05 grm. of V_2O_5).

1.35. Perfectly normal.

4.40. Rather sluggish.

March 24.

9.30. Is very sluggish. Has characteristic lachrymation and diarrhœa. Will not eat.

12.0. Has not moved since last report.

3.0. Is obviously dying.

4.30. Quite dead.

RAT β.
Pyro-vanadate of Sodium.
March 23, 1876.
Weight of Rat 143 grammes.

At 12 h. 20 m. P.M. Injected 1 cc. of standard solution of $Na_4V_2O_7$ (containing V=0·05 grm. of V_2O_5).

12.40. Sluggish; respiration jerky and slow.

1.30. Lies on its side, disinclined to move.

1.40. Noticed to have diarrhœa; fæces green, pulpy and contain much mucus.

2.5. In a very drowsy, sluggish state; respiration gasping and uneasy.

4.20. Lying on its side; motionless when touched. Respiration very difficult and slow.

March 24.

9.20 A.M. Found dead.

These four complete sets of experiments demonstrate in a very conclusive manner the fact which we have ascertained by many other experiments, that the poisonous activity of ortho-vanadate of sodium is much less than that of the pyro- or meta-vanadates of the same base.

Although the poisonous activity of vanadium appears to differ in these compounds, their fundamental mode of action is the same; in all its compounds vanadium appears to exert its chief action on the medulla oblongata and spinal cord, rapidly impairing the action of the various centres situated in the former, whilst it interferes in the most marked manner with the reflex action of the latter; in all its compounds it retains its actions as an irritant of the alimentary mucous membrane, and as an agent exerting a definite poisonous action upon the intrinsic nervous mechanism of the heart.

Any speculations as to the cause of the difference of activity of vanadium in the various vanadic acids will be most suitably discussed in relation with the new facts which have been recently discovered in this Laboratory, as to the radical differences in the action of ortho-, pyro-, and meta-phosphoric acids.

ON THE DIFFERENCE IN THE POISONOUS ACTIVITY OF PHOSPHORUS IN ORTHO-, META- AND PYRO-PHOSPHORIC ACIDS. By Professor Arthur Gamgee, M.D., F.R.S., John Priestley, *Assistant Lecturer in Physiology and Histology in Owens College,* and Leopold Larmuth, *Platt Physiological Scholar, Owens College.*

(*From the Physiological Laboratory of Owens College.*)

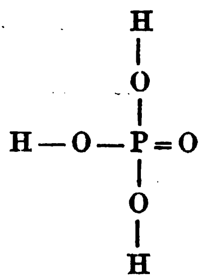
When experiment had shewn that vanadium exerts a different poisonous intensity according as it exists in ortho-, meta- and pyro-vanadic acids, it occurred to us that it would be of great interest to determine whether any similar difference would be manifested by the much better known corresponding phosphoric acids.

Phosphorus pentoxide (or, as it used to be called, anhydrous phosphoric acid) may be made to combine with the elements of water and to yield three most interesting acids, which used formerly to be represented as three hydrates of phosphoric anhydride, and which have, since the researches of Graham made them known to us, been distinguished by the names of ortho-, pyro- and meta-phosphoric acids.

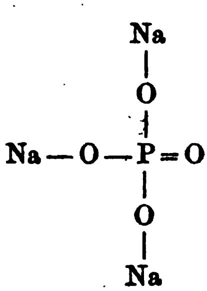
Ortho-, common, or tribasic phosphoric acid used formerly to be known by the rational formula $3HO.PO_5$, which represented it as a compound of PO_5 with three molecules of water; making use of the higher atomic weights which we now universally employ, that formula becomes $3H_2O.P_2O_5$. The fact that ortho-phosphoric acid may be obtained by a direct combination of P_2O_5 and $3H_2O$ does not however warrant the assumption that ortho-phosphoric acid is a compound in which water is linked to P_2O_5; indeed that assumption is disproved by a variety of considerations, and we now write the formula of ortho-phosphoric acid H_3PO_4, which merely indicates that it is an acid which possesses three atoms of H replaceable by three atoms of a

monatomic metal. We may represent the constitution of ortho-phosphoric acid by the formula $(HO)_3PO$, by which we indicate that ortho-phosphoric acid is a compound of the oxygenated radical PO with three atoms of hydroxyl, which may be replaced by one, two, or three atoms of a univalent radical such as NaO.

The following graphic formulæ represent the structure of ortho-phosphoric acid according to this view, and that of normal sodium ortho-phosphate, which is of interest to us as having been used in our research:



$(OH)_3PO$ or H_3PO_4

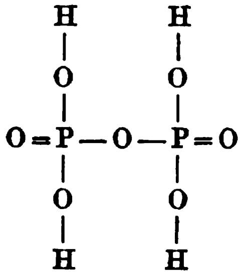


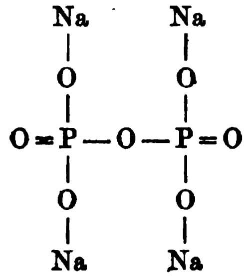
$(NaO)_3PO$ or Na_3PO_4

From ortho-phosphoric acid, by the aid of heat, we can obtain pyro-phosphoric acid, which used to be represented by the formula $2HO.PO_5$ (*i.e.* with the present atomic weights $2H_2O.P_2O_5$), and by the still further application of heat meta-phosphoric or glacial phosphoric acid is obtained.

According to the old view pyro-phosphoric acid was a compound of two molecules of water with one of P_2O_5 and was a dibasic acid. This view of its constitution is certainly incorrect. Pyro-phosphoric acid is a tetrabasic acid, represented by the empirical formula $H_4P_2O_7$, and which may be represented by the constitutional formula $P_2O_3(HO)_4$.

The following graphic formulæ represent the constitution of pyro-phosphoric acid and normal sodium pyro-phosphate:

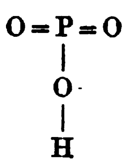


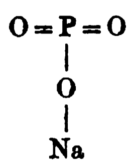


$H_4P_2O_7$ or $P_2O_3(OH)_4$ $Na_4P_2O_7$ or $P_2O_3(NaO)_4$

Meta-phosphoric acid used to be represented by the formula $HO.PO_5(H_2O.P_2O_5)$, indicating the presence in it of a molecule of water and a molecule of phosphoric anhydride. We now represent it by the empirical formula HPO_3; thus whilst H_2O and P_2O_5 may be obtained on heating the acid, water is not contained in the molecule of the acid, of which two molecules are required in order to furnish one molecule of H_2O.

Meta-phosphoric acid may be represented by the rational formula $PO_2(OH)$, and the graphic formulæ of the acid and of its normal sodium salt may be exhibited thus:





$PO_2(OH)$ $PO_2(ONa)$

Meta-phosphoric acid. Sodium meta-phosphate.

It would naturally be out of place here to describe the methods of preparation, the properties, or the reactions of the three phosphoric acids; the few remarks which we have made on their constitution are to remind our readers of the changes which have occurred in our views of the relation of these compounds, which although genetically related must be looked upon as three distinct phosphorus compounds, in which, in spite of

the fact that they can all be resolved into phosphoric anhydride and water, we probably have three separate oxidized radicals, of different structure. After describing our experiments we shall add some theoretical considerations to try and establish some relation between the constitution and physiological action of the phosphorus compounds under examination.

Historical details. Of the three compounds of phosphorus which interest us only one has hitherto been examined in its relations to the animal economy, viz. ortho-phosphoric acid, and it has been found to have the action of other strong mineral acids when administered uncombined and in a concentrated state[1].

We know of no physiological experiments performed with any of the salts of ortho-phosphoric acid. One of these, disodium hydric phosphate, is officinal, and is used in medicine. The experience of physicians has shewn that this salt is destitute of any active physiological action[2]; when administered in large doses, as from 15 to 30 grammes, it acts as a mild purgative; the mildness of its action and a belief in its exerting a special action on the liver and pancreas[3] has caused it to be used of late years as a mild laxative for children.

Plan of the present research. In investigating the special physiological action of any poisonous acid it appears essential, in the first place, that a compound of the acid with an inactive metallic radical should be selected; for, whilst all facts tell us that the specific action of a poisonous acid is retained in such a compound, we know that in virtue of its mere uncombined state any acid will exert such an immediate action upon the physical structure and even the chemical constitution of the solids and liquids of the body as to mask any special physiological action which the acid may possess. Leaving aside the case where acids are introduced into the body in such large quantities that they exert a corrosive or solvent action on the parts with which they come in contact, we know that if an acid or a salt of acid reaction be introduced into the blood in a quantity at all greater than suffices to neutralize the feeble alkalinity of that fluid, we

[1] Hermann, *Lehrbuch der experimentellen Toxicologie.* S. 158.
[2] Nothnagel, *Handbuch der Arzneimittellehre.* Zweite Auflage. S. 213.
[3] Stephenson, *Edinburgh Med. Journal*, 1867, Vol. XIII. p. 836.

have at once an energetic decomposition of the blood-colouring matter, which splits up into hæmatin and a proteid body, besides precipitation of proteids contained in the plasma which are held in solution by the alkalis contained in that fluid. When such changes are induced it is needless to say that we may seek in vain for the specific results of the physiological action of the substance which has led to their occurrence.

In order to obviate any effects which might depend upon mere acidity and to make our experiments comparable, we usually experimented with the solutions of pure trisodic ortho-phosphate, tetrasodic pyro-phosphate and sodium meta-phosphate, in most of our experiments making use of standard solutions which contained the same amount of phosphorus, calculated as P_2O_5.

Our experiments were performed on frogs, rabbits, and dogs, and the drugs investigated were generally introduced into the system either by injecting their solutions subcutaneously or into the veins. They will be divided into three series; only those experiments are quoted which are required to bring out prominently the fact of the great difference in poisonous intensity which exists between ortho-, meta- and pyro-phosphoric acids, all the experiments which specially elucidate the action of pyrophosphoric acid as a poison of the circulation being reserved for a separate communication.

EXPERIMENTS ON SODIUM ORTHO-PHOSPHATE.

EXP. I. A solution of pure crystallized disodium hydric phosphate ($Na_2HPO_4 + 12H_2O$) made, containing 2·5 per cent of P_2O_5.

H. M.
1 . 55. Injected 1 cc. of this solution under the skin of a small frog weighing 14·29 grammes.

After the injection the frog appears quite active and leaps away.

H. M.
2 . 10. Frog is quite lively, leaping about under the bell-jar.
2 . 15. No perceptible effects; frog appears quite lively.

The frog was observed at intervals till 5h. 10m., no poisonous action being noticed; it was then placed in the trough, and the following morning it was found in a perfectly normal condition.

EXP. II. (1 | 3 | 76.)

H. M.
12 . 13. Injected 2 cc. of the same standard solution of sodium

ortho-phosphate under the skin of a frog weighing 20·655 grammes; after the injection the frog leaps away actively.

12 . 55. The frog appears perfectly normal. After this the frog was watched carefully until 6 p.m., when it was placed in the trough; on the following morning it was found to be perfectly normal.

EXP. III. (12 | 3 | 76.) A rabbit weighing 1838 grammes had its left carotid connected with the kymographion, and three separate quantities of solution of ortho-phosphate of sodium were injected into the right jugular vein.

The solution contained 2·5 per cent. of P_2O_5 as tri-sodium ortho-phosphate, and the quantity injected each time was 2 cc., so that in all 0·15 grm. of P_2O_5 as ortho-phosphate was injected. Between the 1st and 2nd doses the interval which elapsed was 8 minutes and 5 seconds, between the 2nd and 3rd 26 minutes and 40 seconds. Throughout the whole experiment no appreciable change occurred in blood-pressure, in number or character of heart-beats.

Without quoting the actual notes of the experiment in detail, we may illustrate the statement by giving the arterial pressure and heart-rate for 10 seconds before the 1st injection of the drug, after the 2nd and 3rd.

H. M. S.				
1 . 29 . 0.	Before 1st injn. arterial pressure		85 mm.	P. 52 in 10 secs.
1 . 37 . 35.	After 2nd injection	ditto	85 mm.	P. 52 in 10 secs.
2 . 4 . 20.	After 3rd injection	ditto	83 mm.	P. 52 in 10 secs.

This rabbit was released and appeared perfectly normal after the experiment. It was, as an exception to our usual laboratory rule, allowed to live, in order that its state might be watched. It continued perfectly normal, and on the 20th March, being in perfectly good health, it was subjected to the action of sodium pyrophosphate.

EXP. IV. A vigorous rabbit, the weight of which was unfortunately not ascertained, was experimented upon as the one in Exp. III. In this case 12 injections of the same solution of sodium ortho-phosphate, each of 1·75 cc., were made into the jugular vein, so that in all 21 cubic centimetres of a solution of ortho-phosphate containing 0·25 per cent. of P_2O_5 were introduced into the circulation, but, as will be seen from the following data, there was no perceptible effect produced either upon blood-pressure or heart-beats.

Time. H. M. S.		Blood Press.	Plse. in 10 secs.
12 . 57 . 15.	Before 1st injection	134	48
1 . 12 . 45.	After 4th injection	128	38
1 . 24 . 30.	After 8th injection	138	40
1 . 33 . 0.	During 12th injection	124	44

No phenomena of any kind were observed to be produced by the injection into the blood of this rabbit of sodium ortho-phosphate containing 0·525 grm. of P_2O_5.

The experiments which have been narrated shewed that sodium ortho-phosphate was apparently an inert substance, contrasting, as will be seen, in a very marked manner with sodium pyro-phosphate.

For reasons which will appear obvious in the sequel, the following experiments were performed:

Exp. V. (10 | 3 | 76.)

H. M.	
3 . 0.	Heart of Rana temporaria prepared for Coates' experiment. Connection made with serum reservoir and gauge. Reddish and fresh rabbit's serum used.
3 . 20.	Normal tracing taken. Heart is beating vigorously 6 times in 10 seconds.
3 . 30.	A second tracing taken; exactly same as first. Serum now mixed with 1-24th of its volume of a standard solution of Na_3PO_4 containing 5 per cent. of P_2O_5.
3 . 35.	Heart beats with great vigour and perfect regularity.
3 . 50.	Tracing again taken. Heart beats very vigorously, only about 3 times in 10 seconds.
4 . 30.	Heart still beating vigorously 4 times in 10 seconds.
5 . 50.	Heart still beating vigorously 4 times in 10 seconds.

Exp VI. (14 | 3 | 76.) Rana temporaria prepared for Coates' experiment.

H. M.	
1 . 10.	Tracing taken. Heart beating normally 5—6 times in 10 seconds.
2 . 10.	Another normal tracing taken. Heart still beats 5—6 times in 10 seconds.
2 . 15.	The pure serum replaced by a mixture of 1 volume of standard solution of Na_3PO_4 and 9 volumes of reddish rabbit's serum.
2 . 20.	Ventricle contracting imperfectly and irregularly. A tracing taken which is but a wavy line.
2 . 30.	Heart beating more perfectly than before, still slowly.
2 . 40.	Ventricle now again contracts with very great vigour, and contraction lasts long. About 2 contractions in 10 seconds.
3 . 30.	Ventricle still contracting energetically, but very slowly and somewhat irregularly.

Experiments on Sodium Meta-phosphate.

In these experiments a solution containing $NaPO_3$ was made. The P calculated as P_2O_5 amounted to 5 per cent. It therefore

contained in an equal volume twice as much P as the solution of ortho-phosphate employed in Experiments 1 to 6.

EXP. VII. (13 | 3 | 76.)

H. M.
3 . 30. A vigorous specimen of Rana temporaria weighing 33·72 grammes had 1 cubic centimetre of the standard solution of sodium meta-phosphate injected under the skin. The frog leaped away vigorously after the injection.
3 . 35. Frog appears to be in a perfectly normal condition.
3 . 40. No perceptible change in the frog.
3 . 50. In same state as before.
4 . 40. Is sluggish: does not move at once when touched. Partial paralysis of hind limbs.
5 . 50. Very sluggish. Lies on belly with hind limbs extended. Reflex action is impaired but not abolished.

The frog was then placed upon moistened filter paper under an inverted funnel. On the morning of the 14th the frog was found to have apparently recovered.

EXP. VIII. (12 | 3 | 76.) A rabbit weighing 1794 grammes.

H. M.
4 . 0. Injected 1 cc. of standard solution of sodium meta-phosphate into left external jugular vein. No change in the animal's condition resulted.
4 . 52. Injected 1 cc. more of solution. After it appears absolutely normal.
5 . 20. Injected 2 cc. of solution (= 0·10 grm. of P_2O_5). No change.
6 . 0. Appears in perfect health. Is eating. The wound was stitched up and the animal recovered.

EXP. IX. (20 | 3 | 76.) Rabbit weighing 1678 grammes.

H. M.
3 . 40. The rabbit being quite well and its temperature 39·4°, 5 cc. of standard solution of sodium meta-phosphate (containing P corresponding to 0·25 grm. of P_2O_5) were injected under the skin. No symptoms were noticed.

The following day, 21st March, 1876, at 10 a.m., the animal seemed normal. Temp. 39·2°. Respirations appear slow.

By an accident one of this rabbit's legs was broken and it was killed.

Sectio Cadaveris. Liver greyish throughout, friable; not decidedly, but doubtfully fatty. Kidney mottled extensively with white; medullary portion congested; cortical portion swollen; renal epithelium somewhat cloudy. Bladder filled with brown thick urine, which was albuminous.

EXP. X. (14 | 3 | 76.) Rana temporaria prepared for Coates' experiment. Fed with reddish rabbit's serum.

H. M.
3 . 50. Normal tracing taken. Heart is beating regularly and vigorously 5—6 times in 10 seconds. Tracing taken.
4 . 30. Heart beating still regularly. Another tracing taken and found not to differ sensibly from the last.

Pure serum now replaced by a mixture of 1 volume of standard solution of meta-phosphate and 25 volumes of serum.

H. M.
4 . 32. Ventricle hardly contracting. Is distended; cannot get a tracing. Auricles contracting.
4 . 45. In same state as before. Auricles contracting imperfectly 10 times in 30 seconds. Direct mechanical excitation does not cause the ventricle to contract.
4 . 48. Auricle contracting 11 times in 30 seconds.
5 . 15. Ventricle as before. No contraction on excitation. Auricles contracting very feebly 11 times in 30 seconds.

EXPERIMENTS WITH SODIUM PYRO-PHOSPHATE.

In this series of experiments solutions of pure sodium pyrophosphate were prepared either by dissolving the crystallized salt, $Na_4P_2O_7 + 12H_2O$, or the anhydrous salt obtained by igniting the above.

EXP. XI. (29 | 2 | 76.)

H. M.
12 . 20. An active English frog weighing 16·4592 grms. had 1 cub. cent. of a standard solution of sodium pyro-phosphate injected under the skin of the back. The solution of pyrophosphate corresponded to 2 per cent. of P_2O_5.
12 . 40. Appears quite active, leaping about under the large funnel by which it is covered.
12 . 50. Struggles as if attempting to leap, but unable.
1 . 2 . 5. Lies with limbs extended. No movement on pinching toes.
1 . 25. Frog appears dead. Limbs are perfectly flaccid and motionless. No reflex action on exciting the skin.
1 . 27. Left sciatic exposed. Excited by weak induction shocks of Du Bois Reymond's induction coil. With secondary coil at 28 centimetres from primary, muscles contract well.
1 . 33. Upon exposing the heart it is seen to be engorged with venous blood and beating regularly 15 times in 30 seconds.
1 . 55. Upon galvanizing the left sciatic muscular contraction still takes place.
2 . 15. Movements of leg still occur on exciting sciatic.

Exp. XII. (29 | 2 | 76.)

H. M.

2 . 7. Injected 2 cc. of the same solution of pyro-phosphate of sodium under the skin of a healthy R. temporaria weighing 22·32 grammes.

2 . 30. Frog sprawls; cannot support itself on its anterior extremities.

2 . 35. Lies passive and flat. When hind limbs are extended does not draw them forwards. Still possesses apparently some slight power of voluntarily moving its body. There is in fact a state of paresis, if not of paralysis.

3 . 10. Frog perfectly flaccid. Reflex action found to be completely abolished when limbs are dipped in dilute H_2SO_4.

3 . 15. Upon exposing left sciatic and exciting by means of weak induction shocks (secondary coil of Du Bois Reymond's apparatus at 28) twitching of the legs occurs.

4 . 25. Heart exposed and found to be beating feebly but regularly 14 times in 30 seconds.

Exp. XIII. (2 | 3 | 76.)

H. M.

9 . 56. A very active R. temporaria weighing 39·49 grms. had 1 cc. of the same solution of $Na_4P_2O_7$ injected under the skin.

10 . 15. Frog very inactive.

10 . 20. Frog sprawls. On pinching hind legs they are fully drawn up.

10 . 40. Frog in a very sluggish state, still after posterior extremities have been extended they are slowly drawn up.

10 . 50. Frog lies perfectly flaccid.

11 . 0. In same state as before. No reflex movements when toes are pinched.

11 . 30. Frog lies perfectly flaccid. Reflex action tested by dipping legs into dilute H_2SO_4, and found to be abolished.

11 . 35. Heart exposed. Is engorged with very venous blood and beats regularly 17 times in 30 seconds.

11 . 50. Heart beating very slowly and imperfectly.

12 . 15. Heart in a very distended state: scarcely pulsating.

Exp. XIV. In this experiment a rabbit weighing 2535 grammes was employed. 2·5 cc. of the standard solution of sodium pyrophosphate, as used in the last experiments, was mixed with 5 cc. of sheep's serum.

H. M.

4 . 1. 2 cc. of this mixture injected into the external jugular vein.

4 . 5. Injection completed. No convulsions or movements.

4 . 20. Appears normal.

5 . 0. Seems quite normal.

5 . 2. Injection of other 2 cc. commenced.

5 . 5. Injection completed. No convulsions. Appears drowsy (?).

5 . 33. Injected nearly, but not quite, 2 cc.
5 . 35. Stretching convulsions. Paralysis of hind limbs.
5 . 38. Severe stretching convulsions. Eyes insensitive. Gasping respiration.
5 . 40. Tremors of lips.
5 . 50. *Sectio cadaveris.* Right heart is distended; auricles are beating.

EXP. XV. Rabbit weighing 2265 grammes.

H. M.
12 . 16. Respirations 20 in 10 seconds.
12 . 51. Injected 2·5 cc. of same solution of sodium pyro-phosphate (this quantity of solution contains $P = \cdot 05$ grm. of P_2O_5) into the external jugular vein. Struggles; when released moves about normally. Respirations 11—13 in 10 secs.
1 . 9. Seems normal; if anything is rather drowsy.
1 . 15. Respirations 10 in 10 seconds. Heart beats 40—44 in 10 seconds.
1 . 38. Injection of 5 cc. of the solution ($= \cdot 10$ grm. of P_2O_5).
1 . 39. Most severe convulsions, opisthotonos; clonic, stretching convulsions. Cornea insensitive. Respiration rapid and powerful.
1 . 41. Cornea quite sensitive again. Complete paralysis of posterior but not of anterior extremities. Respirations 36, 34, 33, and 34 in 10 seconds. Hind limbs now lax and quite paralyzed. No reflex action follows pinching any portion of skin, but movements of eyelids follow irritation of the cornea.
1 . 46. Heart beats 40 times in 10 seconds. On touching its fore-legs the rabbit moves its eyelids but not its limbs. Paralysis of whole body except head.
1 . 49. No alteration of eye on pinching the legs. Attempts to move in a wriggling manner. Sharp slight opisthotonic movements. Opisthotonos. Cessation of respiration. Pupils dilating. Stoppage of heart.
1 . 52. Is quite dead.
1 . 57. *Sectio cadaveris.* Slight movements of heart, the cavities of which, especially the right, are gorged with blood. Vermicular movements of intestines are proceeding actively. Intestinal vessels are much injected with blood.

EXP. XVI. (15 | 3 | 76). Rabbit weighing 1595 grammes.

H. M.
1 . 55 p.m. 12·5 cc. of a solution of sodium pyro-phosphate solution (containing P=2 per cent. of P_2O_5) diluted with 8 cc. of water were injected under the skin of the left side.
3 . 30. The rabbit is lying down and appears normal.
4 . 25. Crouches or lies as if sleepy; otherwise is normal.

March 16.

9 . 30 a.m. Rabbit appears weak and ill; sniffles in breathing. Can walk, but is weak. Respiration 5—6 in 10 seconds, deep.
2 . 47. Temperature in rectum 35·6° C.
5 . 30. The same state as before.
9 . 37. Respiration 5–6 in 10 seconds.
10 . 45. Condition remains unaltered. Drinks greedily.

March 17.

11 . 30 a.m. Temperature in rectum 34·1° C. Lies on its side unable to stand. Bladder emptied by pressing abdomen. 28 cc. of urine were obtained; reaction acid; contains a large quantity of albumen; contains a doubtful trace of bile-colouring matter and no sugar. Chlorides appear deficient.
1 . 28. Respirations 10 in 10 seconds. Cannot stand.
1 . 38. Found dead.

Sectio cadaveris. On dissecting the skin from the middle line of the abdomen the cellular tissue is found to be œdematous, so that large quantities of fluid trickle away. Auricles and ventricles of heart have ceased to beat. Both sides of the heart contain blood, which coagulates on exposure. Lungs normal. No appearance of peritonitis. Intestinal peristalsis still going on. Stomach contains a small quantity of food. On opening it a few doubtful punctiform extravasations were seen. Duodenum contained much greenish gelatinous mucus. Its upper part presents injection of the mucous membrane. Small intestine appears injected throughout its entire length. Liver appears normal. Right kidney is fatty; left not markedly so. Bladder contains some urine.

Exp. XVII. (20 | 3 | 76.) Rabbit weighing 1813 grms.

H. M.
1 . 0 p.m. Temperature in rectum 39·8° C. Injected 6·25 cc. of standard solution of $Na_4P_2O_7$ below the skin (the P in this quantity is equal to 0·125 grm. of P_2O_5).
1 . 15. Seems slightly uneasy.
5 . 30. Lies quiet.

March 21.

10 . 0 a.m. Appears to be in a normal condition.
11 . 45. Temperature in rectum 38·5° C.
5 . 40. Has eaten well, and seems in good health. T. 38·4°. Again injected 6·5 cc. of same solution.

March 22.

9 . 30. Seems normal; perhaps a little quieter than usual.
1 . 25. Appears normal. T. 39° C. Respirations 17 in 10 seconds.
4 . 0. Temperature 39° C.
4 . 50. Injected 6·5 cc. of same solution under skin.

March 23.

8 . 30 p.m. Temp. 38·6°. Respiration 10 in 10 seconds and irregular. Apparently some cellulitis where injections have been practised.

8 . 53. Injection 6·25 cc. of same solution. The rabbit is losing flesh; it eats, but not greedily.

March 24. Seems very quiet; has eaten all its food.

12 . 45 p.m. Respiration 7 in 10 seconds and very shallow. Temp. in rectum 38·1° C.

March 25.

1 . 0 p.m. Temperature 39·2° C. Is very thin. Has had diarrhœa. Drinks greedily.

1 . 30. Respirations 9 in 10 seconds, jerky and irregular.

March 27.

10 . 0 a.m. Seems much brighter, eats and drinks greedily. Moves about with alacrity, and evinces interest in what transpires around it. Respiration 9—10 in 10 secs. Temp. 38·8° C.

4 . 30. Repeated injection of 6·5 cc. of standard solution.

March 28. Lies on its side. Moves fore-legs normally.

9 . 30 a.m. Cannot stand up. Anterior half of body appears hyperæsthetic. Respiration 9 in 10 seconds. Temp. 37° C.

12 . 0. Still lies on its side. Nibbles its food eagerly.

5 . 40. Temperature in rectum 37·1° C. Fæces are light brown but firm.

March 29. Noon. Died.

Sectio cadaveris. Extensive effusion into the connective tissue, which in parts was indurated. This was not accompanied by congestion and no tendency to the formation of pus.

Stomach quite empty of solid food, but contains a bright green fluid (!). Exhibits on its mucous membrane a few brown hæmorrhagic spots and patches. Small intestine contains yellow contents, viscid and turbid. On serous surface of intestine a few slight blood extravasations are noticed. Peyers' patches are quite normal. Vermiform appendage quite normal. Large intestine normal. Kidneys large and white; much congested, very friable. Medullary portion of kidney swollen. 'Grenzschicht' congested. Bladder contained thick and muddy urine with an abundant sediment containing a large number of very fatty cast mixed with phosphates. Liver dark-coloured, but fatty. Heart somewhat fatty. Clear coagulum in auricles. Lungs normal.

Exp. XVIII. Rabbit weighing 1835 grms.

March 14, 1876.

3 . 45. Injected under the skin a solution of 3·14 grms. of anhydrous $Na_4P_2O_7$.

3 . 55. Very excited. Tendency to fall over on its side.
4 . 0. Respiration 26 in 10 seconds.
4 . 18. Respirations 14, 15, 16 in 10 seconds.
5 . 0. Respirations 13 and 14 in 10 seconds.
6 . 10. Lies in corner of hutch. Moves with difficulty.

March 15.

8 . 30 a.m. Found dead and quite rigid.
11 . 30. *Sectio cadaveris.* Intense congestion of abdominal muscles and infiltration of subcutaneous connective tissue of the right side of abdomen and back. Mesenteric vessels injected. Stomach presents intense brown patches at the cardiac and back wall, together with a general redness near the œsophageal end. Intestines filled with thin, gruelly contents. Vermiform appendage congested. Spleen normal. Kidneys normal, liver not fatty. Heart much distended on right side. Left ventricle contracted. Lungs not congested. Bladder firmly contracted.

In order to avoid the repetition of experiments, we shall not here quote any experiments with serum poisoned with sodium pyro-phosphate, by Coates' method, although these experiments are needed to allow of a comparison between the experiments of series I, II, and III. As the Coates experiments are quoted in the paper in which we treat of the special action of sodium pyro-phosphate as a poison of the circulation, we shall here only state their results. Sodium pyro-phosphate exerts upon the frog-heart exactly the same action as sodium meta-phosphate, except that it is, if anything, rather more energetic, *i.e.* when 1 volume of a solution containing P corresponding to 2 per cent. of P_2O_5 is mixed with 25 volumes of rabbit's serum, and the mixture is made to circulate through the heart, the ventricle is at once arrested, becoming powerfully contracted, whilst the auricle continues to beat though with great feebleness.

Having stated the main facts of our researches, it will be well that we should point out the general conclusions.

It results from our observations that ortho-phosphoric acid in combination with sodium is a substance which is destitute of any marked physiological activity. When taken into the alimentary canal of man it produces no marked result, save that which appears to follow the injection of other inert neutral alkaline salts. When injected under the skin of frogs, these most susceptible animals remain perfectly unaffected, and no result is observed when large quantities are introduced directly into the veins of rabbits. The only result which may be called a positive result was obtained when serum containing a large quantity of sodium ortho-phosphate was made to circulate

through the frog's heart. It was found that although the heart went on beating, even for hours, the pulsations were slower than normal and altered in character. These changes however are fully accounted for by the amount of the sodium salt present in the serum, and which must in a most marked manner, by diffusion, have initiated physical changes in the frog's heart. The slowing of the heart, with powerful lengthened systoles, is observed by Coates' method when serum which is not quite adapted to the frog's heart (*e.g.* sheep's serum) is used.

With regard to meta-phosphate of sodium, our experiments conclusively shew that it is a poisonous substance, although not by any means as poisonous as sodium pyro-phosphate. It appears to share the action of the latter as a direct poison of the heart.

Pyro-phosphate of sodium is shewn to be a substance of great poisonous activity. Our experiments have clearly demonstrated that in its action on frogs it is more poisonous than sodium ortho-vanadate, having about the same intensity as sodium pyro-vanadate. In rabbits, when introduced into the circulation, it is very poisonous, although its action is certainly not so marked as that of the corresponding vanadium compound.

When we glance at the symptoms induced by sodium pyrophosphate, we find that it is a poison which induces death without materially affecting the irritability of voluntary muscles or of nerves. It exerts an action on the spinal cord and medulla oblongata, which resembles most closely that of vanadium compounds. Upon the heart too its action is very similar to that of vanadium. Upon the alimentary canal sodium pyrophosphate has in some cases appeared to exert no marked action. In others it has induced appearances identical with those observed in some cases of phosphorus poisoning. In its effects on the general nutrition the poison has shewn great resemblance to the poisonous element phosphorus which it contains, for in cases where death has been delayed there has been very marked fatty degeneration of the kidneys, of the muscular substance of the heart, with slighter degeneration of the liver.

In the account which we have given of the action of pyro-

phosphoric acid, we have not attempted to state the results of all our researches, much less have we pretended to give a complete account of the physiological action of the body. We must, however, allude to one result which has surprised us, and which we hope to elucidate by fresh experiments. We have never succeeded in producing symptoms of poisoning by sodium pyro-phosphate when we have introduced the substance into the stomach. In dogs the drug has produced vomiting but no further ill effect; rabbits have remained unaffected by it; so striking was this absence of poisonous symptoms that it appeared to us possible that some of the alimentary ferments might cause sodium pyro-phosphate to combine with the elements of water, and convert it into the inert ortho-phosphate; direct experiments, in which salivary, gastric, and pancreatic ferments were digested with pyro-phosphate at the temperature of the body, proved that our surmise was not correct. At present we are inclined to think that the fact of animals not being poisoned when sodium pyro-phosphate is introduced into their alimentary canal is due to the rapid elimination of the drug.

Whilst we are, as at present, so thoroughly in the dark as to the conditions of poisonous activity—for we do not know in virtue of which physical or chemical properties the molecules of a poisonous body interfere with the physical properties or the chemical structure of the elementary tissues and organs, and so lead to those disturbances of function which constitute poisonous action—it may appear premature to speculate on the causes of the inactivity of phosphorus in most of its compounds, an inactivity which demands explanation.

Whilst arsenic, antimony, and vanadium exert their characteristic actions on the alimentary canal, on the nervous system, on general nutrition, almost irrespective of their state of combination, phosphorus fails to impart to many of its compounds any poisonous activity; indeed it can scarcely be said to exert what we may term its elementary action, except when uncombined, and then only when in the condition of yellow phosphorus.

We need not seek for a better example of an inactive phosphorus compound than is furnished by sodium ortho-phosphate, which we have conclusively proved to be physiologically a per-

fectly inert body. Why should phosphorus in Na_3PO_4 be inert, whilst vanadium and arsenic exert their characteristic action with energy in the corresponding arseniate and vanadate?

If the poisonous action of poisonous elements be due to definite chemical operations performed by them in the body, *i.e.* if for its development the elements have to take part in chemical reactions, it is quite conceivable, as indeed Hermann has hinted, that the compounds of arsenic or antimony should be more poisonous than those of phosphorus, for they are much more unstable. We know, for example, with what ease compounds of arsenic and antimony take part in reactions which do not succeed with phosphorus; the action of zinc and sulphuric acid on an antimoniate, an arseniate, and a phosphate, offer a good illustration of this difference. In the two former cases the nascent hydrogen is capable of attacking the Sb and As to form their gaseous hydrides; in the latter the phosphorus is so firmly linked to oxygen that the attack fails. Similarly we may conceive that in the body an ortho-phosphate will escape all fundamental decomposition; its phosphorus will never present itself in any chemical operation except in the condition of a saturated compound.

We do not believe that we are outstepping the limits of justifiable scientific speculation in assuming that a poisonous element will be unable to exert its characteristic *elementary* poisonous properties unless it can itself take part in chemical reactions, and this it will not be able to do if it passes through the body with all its affinities saturated; we do not by this mean to imply that no saturated compound can, in its passage through the body, exert an action unless it be decomposed, for it is probable indeed that the activity of many organic bodies is really due to an action of their undecomposed molecules upon the molecular structure of tissues and organs.

Our contention is that the action of an element itself, say As, V, or Sb, or P, will not be manifested except it enters into reactions which shall for the time leave some of its affinities unsaturated. How can we explain the inactivity of cacodylic acid, which contains about one half of its weight of arsenic, except by supposing that in this saturated compound the arsenic is so securely linked to carbon and oxygen atoms, that in no

reaction of the body does it present affinities to be saturated—that in no reaction does it appear as arsenic? On the other hand, we can easily understand how in the much more complex molecule of cacodyl the affinity which links arsenic to arsenic should be overcome with considerable ease, leaving the unsaturated arsenic atoms to exert their full action upon the elementary organs where the decomposition occurs.

In pyro-phosphoric acid and the pyro-phosphates we have examples of bodies of much greater complexity than the ortho-phosphates, and in which the phosphorus is not fully saturated. We can readily understand that such a body as pyro-phosphoric acid might, either in its integral condition (in virtue of the state of the phosphorus of its molecule) attach itself to other bodies and exert a specific phosphorus action, or that it might in the body undergo decomposition, and at the time of decomposition be in a fit state to enter into chemical reactions.

Similarly in meta-phosphoric acid phosphorus affinities are not as fully satisfied as in ortho-phosphoric acid, and the body is one which would presumably exert a greater action than ortho-phosphoric acid.

ON THE ACTION OF PYRO-PHOSPHORIC ACID ON THE CIRCULATION.

By PROF. GAMGEE, M.D., F.R.S., JOHN PRIESTLEY, *Assistant Lecturer in Physiology in Owens College*, and LEOPOLD LARMUTH, *Platt Physiological Scholar, Owens College.* (Pl. IX.)

(*From the Physiological Laboratory of Owens College.*)

WE have already drawn attention to the interesting fact that whilst sodium ortho-phosphate is a substance possessing no activity as a poison, the meta-phosphate is undoubtedly poisonous, and the pyrophosphate still more so. The facts which bear upon the general action of the latter compound have been cited, and we have endeavoured to shew that sodium pyro-phosphate exerts an action which, in so far as the nervous system and the circulation are concerned, is very similar to that of the corrresponding vanadium compound.

As we are very much interested in the discovery of the physiological relations which may exist between the different members of the most interesting group of elements to which both phosphorus and vanadium belong, we determined upon making a somewhat exhaustive examination of the action of sodium pyro-phosphate on the circulation of the blood, so as to be able to compare the facts thus obtained with those yielded by the analogous research already conducted with the vanadium compound.

Our experiments have been performed on rabbits and frogs, the latter animals having been employed in studying the direct action of sodium pyro-phosphate on the heart.

In seven cases we have determined, by means of the kymographion, the changes induced in rabbits when sodium pyro-phosphate is introduced into the circulation. Of these seven perfectly concordant experiments, we have given the notes of five. Three experiments illustrate the effects of the salt on rabbits with spinal cord and vagi intact. One experiment shews the changes which occurred when the vagi had been divided; and another exhibits the effects on a curarized

rabbit, of which the cord had been divided at the atlanto-occipital articulation.

EXP. I. Rabbit, 1755 grm. Dose, 1·65 cc. solution of sodium pyro-phosphate, containing 2 per cent. P_2O_5 injected into vein. Kymograph at carotid.

Time.	Pulse in 10 sec.	B. P.	Remarks.
H. M. S.			
1.18	38	111	Normals. Resp. curves 10 in 10 sec.
1.18.12	39	118	Injection commenced.
1.18.19	39		B. P. begins to fall. Pulse slightly irregular.
1.18.20		108	
1.18.21			Pulse becomes extremely slight and slow, and the B. P. falls lower.
1.18.35		69	
1.18.40			Injection complete; at which time struggles or convulsions sent up the B. P. irregularly, keeping it up until 1 h. 18 m. 52 s., after which the heart seemed to cease and the B. P. fell gradually and steadily. Breathing continued, although the heart never went on again.
1.21.30	none	25	Movements occurred, not altering B. P.
1.22.30	none	25	Pinching the legs caused movements of lips.
1.23	none	25	Slight respiratory movements.
1.24	none	25	Movement on pinching hind leg.
			Dead.

EXP. II. (See Plate IX.) Rabbit, 1665 grm. Dose, 3·2 cc. of solution of pyro-phosphate of soda, containing 2 per cent. P_2O_5 injected into ext. jugular vein.

Time.	Pulse in 10 sec.	B. P.	Remarks.
H. M. S.			
			Kymograph at carotid.
4.20.40	44	124	Normals. Resp. curves 5—6 in 10 sec.
4.21.7	44	124	Injection commenced.
4.21.20	44	124	Resp. curves as before.
4.21.22	44		B. P. begins to fall. Pulse a little irregular.
4.21.30	43	102	B. P. gradually falls. Pulse becomes very irregular.
4.21.35	20	80	Pulse large and slow. B. P. gradually fallen.
4.21.37			Struggles send up B. P. Injection complete.
to	23		Struggles send and keep up B. P. Pulse large, slow, and irregular.
4.22			
4.22	22	90	Pulse becomes very slow, and slight.
4.22.30	none		B. P. falls in a sweep to 40 mm.
4.22.40	none	34	B. P. gradually falls. Convulsions occur, not affecting B. P.

EXP. III. Rabbit, 1775 grms. Dose, $\left.\begin{matrix}2 \text{ cc.}\\ 2 \text{ cc.}\end{matrix}\right\}$ of solution of pyro phosphate of soda, containing 2 per cent. P_2O_5 injected into righ ext. jugular vein.

Time.	Pulse in 10 secs.	B. P.	Remarks.
H. M. S.			
			Kymograph at carotid.
4.19.50	49	104	
4.22.55	44	108	Resp. curves 9 in 10 sec.
4.23	44	108	INJECTION OF FIRST DOSE COMMENCED.
4.23.15	28	106	Pulse begins to get slower and less regular.
4.23.20			B. P. begins to fall.
4.23.25		100	Pulse very large and irregular.
4.23.35	22—10	46	B. P. falls quickly, the heart having become extremely slow.
4.23.40			Very severe struggles, sending up the B. P.
to			Heart simultaneously ceases.
			Struggles continue.
4.24.10			Struggles continue.
	22		Heart recommences.
4.24.20			Convulsions occur, raising the B. P. very much.
4.24.30	18	78	B. P. rising. Pulse very large and irregular.
4.24.55	22	112	B. P. steadily rises. Pulse as before. No struggling.
4.25.40	27	110	B. P. steadier. Pulse getting more regular: B. P. presents several marked variations.
4.25.42			Heart ceases again: no struggles occur, and
4.25.46		60	B. P. falls at once to 60 mm.
4.25.48			Heart beats 20 or 30 times, becoming gradually weaker towards the close of the series, during which the B. P. rises again slightly, but falls again as the pulse becomes weaker.
4.26		38	Convulsions which do not at once or violently affect the B. P.
	24		During the next minute the B. P. rises and falls very gradually and regularly three or four times, producing long sweeping curves on the cylinder, varying in height from 30 mm. to 48 mm., during which the heart beats slowly and feebly, but quite regularly.
4.27		48	
4.27.30		82	Convulsions send up the B. P.
4.27.45		88	
4.28			The B. P. irregular but, as a mean, higher.
4.28 to 4.30	47 to 45	86 to 64	Resp. curves now reappear two or three times for about 15 sec., disappearing to give place to a straight B. P. line.
			After this the B. P. became quite normal and finally attained a height of 100 mm.
4.41	47	100	Resp. curves well shewn (12 in 10 sec.). Pulse normal.
4.41.5			INJECTION OF SECOND DOSE COMMENCED.
4.41.15	46	100	Resp. curves well shewn (12 in 10 sec.).
4.41.20	41—42		B. P. begins to fall. Pulse a little irregular and slighter.
4.41.25	20	93	Pulse becomes long and slow: and B. P. begins to fall.
4.41.50	24	62	B. P. gradually fallen. Pulse long (*i.e.* infrequent).
4.42			Opisthotonic convulsions which raise and disturb B. P.
4.43	21	35	B. P. steadily falling. Pulse feeble. Convulsions again follow, with slighter disturbances of B. P.
			Pulse becomes feebler and feebler.
4.45.30		9	B. P. has fallen steadily. Dead.

EXP. IV. *Division of Vagi.* Rabbit, weight 2657 grms. Injec-
n of solution of sodium pyro-phosphate, containing 2 per cent. P_2O_5,
o jugular vein. Carotid connected with kymograph.

Time.	Blood Pressure in mm. mercury.	No. of Respira-tions in 10 secs.	No. of Heart-beats in 10 secs.	Remarks.
M. S.				
0. 0	74	7	40	Normal.
2.52				*Left vagus divided.*
3. 0	92		43	Respiration irregular.
3. 9	122			
3.10	119			
3.12	124			
3.15				*Right vagus divided.*
			43	In next 10 seconds.
3.17	116			
3.20	124			
3.25	139			
3.30	142			
3.35 to 3.40	....	....	....	Struggles.
3.53	148			
4.10	144			
4.20	144	Slow and		
4.45	134	irregular.		
5. 0	132	Generally	42	
5.30	124	2-3 in 10s.		Pressure varies 12 mm. between
6. 0	120		41	inspiration and expiration.
6.20	124			
7.20	120	2	42	
9. 0	112		40	
10. 0	105	3	38	Heart beats irregularly.
10.25		to		INJECTION OF 2 cc. COMMENCED.
11. 0	104		39	Heart very irregular.
12. 0	103	4	38	Still irregular.
13. 0	100			
13.10	96			
13.16	100		36	INJECTION OF 2 cc. $Na_4P_2O_7$ COMPLETED.
13.21	94			
13.30	96			
14. 0	96		34	
14.30	96		39	
15. 0	100		34	
15.15	100		34½	
15.30	104		33	
15.45	104			
16. 0	104			
16.30	104		35	
17. 0	104		34½	
18. 0	100		34½	
19. 0	102		34	
19.21	102			INJECTION OF SECOND 2 cc. OF SAME COMMENCED.
19.30	104		33½	
19.40	103		33	
20. 0	100		32	

Experiment IV. *continued.*

Time.	Blood-pressure in mm. mercury.	No. of Respirations in 10 secs.	No. of Heart-beats in 10 secs.	Remarks.
H. M. S.				
4.20.10	87			Struggles.
4.20.20	86			INJECTION COMPLETED. For next 25 secs. the heart was most irregular; for some 5 s. no elevation perceptible, after that 4 elevations in 10 secs.
4.20.30	70			
4.20.40	67		35½	Steady B. P. curve up and then down.
4.20.53	89			
4.21. 0	64			
4.21.10	48			Steady fall. Line nearly devoid of traces of heart's action.
4.21.20	40			
4.21.25	76			
4.21.33	117		42	Abrupt rise. Heart-beats become again perceptible.
4.21.40	104			
4.21.50	95		41	
4.22. 0	99		36	
4.22.30	104	2—3	38	The respiration-curves here indicate 2-3 in 10 secs.
4.23. 0	114		38½	
4.23.30	110			
4.24. 0	110	4	38	Respirations not counted. Coincidence with respiration-curves only noted occasionally.
4.25. 0	114	5	39	
4.25.30	105	5½	42	
4.26. 0	110	6	44	Pressure very steady.
4.27. 0	110			Respiration regular.
4.28. 0	107	6	40	
4.29. 0	106	5	38	Not so regular. INJECTION OF 1 cc. COMMENCED.
4.29.30	108	5	36	
4.30. 2	106	6	35	INJECTION OF 1 cc. COMPLETED.
4.30.38	98			
4.31. 0	100	6½	35	
4.32. 0	102		32	Heart-beats irregular.
4.33. 0	102			Still irregular.
4.33.50	98		37	" " INJECTION OF 2 cc. COMMENCED.
4.34. 8	96			
4.34.30	98	7½	35	Heart-beats much more regular.
4.35. 0	97	7	36	
4.35.26	82	6	34	Heart very feeble. INJECTION OF 2 cc. COMPLETED.
4.35.45	68			Feeble action, if any, of heart.
4.36. 0	51			
4.36.25	33			Dyspnoea.
4.36.38	70		33 (?)	Heart-beats again perceptible.
4.37. 0	31			
4.37.10	40	4 (?)	38 (?)	Convulsions.
4.37.40	23		over 40 (?)	Steady fall. Heart-beats very faint.
4.38. 0	13			Apparently dead.

Pressure fell rather slowly to zero.

EXP. V. Rabbit, 2088 grms. Dose, 2 cc. of solution of pyro-phosphate of sodium, containing 2 per cent. P_2O_5 injected into ext. jugular vein.

Time.	Pulse in 10 sec.	B. P.	Remarks.
H. M. S.			
			Cord exposed ready for section.
			Kymograph at femoral artery.
4.28	20	84	Normals after all preparations have been made.
4.30	21	94	Injected $\frac{8}{10}$ cc. of 1 per cent. solution urari.
4.30.20			Injection complete (of urari).
4.31.40			Respiration almost ceased.
			Artificial respiration was commenced, 60 times per min., and kept up continuously, the bellows being regulated by means of a watch.
4.38.30	20	95	
4.48	17	120	Cord had been somewhat irritated by bleeding incident to division of the atlanto-occipital membrane. Division of cord. B. P. fell, at first quickly, then more slowly.
4.49	20	63	
4.51.30	23	38	
4.51.40			Injection of 2 cc. of solution of pyro-phosphate of soda commenced.
4.52	23	39	Immediately after this moment the heart begins to slacken, the beats becoming longer (*i.e.* slower), and the B. P. falls steadily.
4.52.20	7	25	Injection complete. Pulse became slower and slower until death.
4.53		14	Heart has ceased.
			Dead.

EXP. VI. Rana temporaria prepared for Coates' experiment. Reddish rabbit's serum used.

H. M.

2 . 40. Normal tracing taken. Heart beats vigorously.

2 . 50. A second normal, exactly similar to the first, taken. Pure serum now replaced by serum mixed with $\frac{1}{24}$th of its volume of standard solution of $Na_4P_2O_7$, containing 2 per cent. P_2O_5.

2 . 51. Auricles beating only 3-4 in 10 seconds. Ventricle contracting feebly at irregular intervals. Cannot get a tracing.

3 . 30. Ventricle tightly contracted; does not respond to mechanical irritation. Auricles continue to beat slowly.

4 . 15. Auricles still contracting slowly and slightly. Ventricles in the same state as before.

EXP. VII.

4 . 0. Rana temporaria prepared for Coates' experiment.

4 . 25. Heart beats well and fully.

4 . 35. Normal tracing taken.

H. M.
4 . 38. Pure serum replaced by mixture of 1 vol. of standard solution of $Na_4P_2O_7$, containing 2 per cent. P_2O_5, and 24 of serum.
4 . 38 . 2s. Ventricle has ceased to contract, or rather has become spasmodically contracted. Auricles beat 4 times in 10 secs.
4 . 50. On touching the ventricle, no contraction is caused; auricles continue beating very slowly.

Exp. VIII.

2 . 30. Rana temporaria prepared for Coates' experiment.
2 . 50. Normal tracing taken. Heart beating vigorously 6 to 7 times in 10 seconds.
3 . 20. Pure serum replaced by mixture of 1 part of sodium pyrophosphate solution, containing 2 per cent. P_2O_5, to 24 of serum.
3 . 21. Cessation of contraction of ventricle in diastole; auricles still beating 15 times in 30 seconds. Cannot get a tracing. Direct mechanical excitation of ventricle does not produce a contraction.
3 . 22. The part of the ventricle which was mechanically excited has now contracted.
3 . 25. Auricles beating sluggishly and feebly 13 times in 30 seconds. Ventricle responds after a long interval to mechanical excitation.
4 . 20. Auricles still contracting feebly 8 times in 30 seconds. Ventricle is distended, and does not respond to irritation.

Exp. IX. Canadian bull-frog, prepared for Coates' experiment. Reddish rabbit's serum used. Right vagus exposed.

H. M. S.
11 . 35 . 0. Ready. Heart, by vigorous beats, pumps the serum rapidly through the circulatory apparatus. Normal tracing taken.
11 . 45 . 0. Second normal tracing taken. Vagus excited. Heart stops in diastole. (Excitation produced by Du Bois-Reymond's apparatus, 1 D., secondary coil at 20 c. m.)
11 . 47 . 0. Serum replaced by a mixture of 24 parts of serum and 1 part standard solution $Na_4P_2O_7$, as above.
11 . 47 . 30. Ventricle not pulsating—firmly contracted. Auricles scarcely contracting.
11 . 47 . 45. Irritation of right vagus; complete stoppage of auricles; no relaxation of ventricle.

On excitation being discontinued the auricles do not recommence, but remain distended. Ventricle firmly contracted; pinching does not produce any results.

The serum was changed, being replaced by normal healthy serum. The heart was emptied of the poisoned serum which it contained, and filled, as far as it was possible, with fresh. Neither auricles

nor ventricle pulsate. Direct stimulation with the current and mechanical irritation each fail to cause contraction.

EXP. X. Canadian bull-frog. Reddish rabbit's serum used. Prepared for Coates' experiment. Right vagus exposed.

H. M. S.	
1 . 0 . 0.	Normal tracing taken. Heart contracts very vigorously and perfectly.
1 . 6 . 15.	Serum replaced by poisoned serum containing 1 part of standard solution $Na_4P_2O_7$ in 75 parts serum.
1 . 6 . 40.	Ventricle stops in systole; auricles continue beating.
1 . 7 . 0.	Vagus excited with electrical arrangements as in preceding experiment (IX.); auricles stop; ventricles do not at all relax.
1 . 8 . 0.	Auricles beat very feebly (8 in 30 seconds). Excitation of the vagus was repeated eight times with the same result, ventricle remaining firmly contracted while the auricles ceased to pulsate. The excitations occurred at intervals of about three minutes.
1 . 15 . 0.	Pulsations of auricles very feeble (5 in 30 sec.). On stroking ventricle with a steel blunt hook slight muscular contractions occurred.
1 . 25 . 0.	Ventricle somewhat more relaxed; no contraction of it on electrical stimulation. Auricles pulsating feebly; they stop on stimulation.
1 . 35 . 0.	Auricles and ventricles both at a stand-still; the latter in the same contracted state as when the next preceding note was made. No contractions follow electrical or mechanical stimulation.

Résumé.

From the experiments which have been quoted, we may arrive at the following general conclusions of the action of pyro-phosphate of sodium on the circulation, when it has been injected into veins.

The symptoms of poisonous action follow within from 6 to 25 seconds of the commencement of injection,—a difference of time, there is no reason to doubt, which is due to the greater or less rapidity of injection, and the less or greater quantity of blood in the blood-vessels of the animal experimented on. During this interval we would merely note that the appearance of the graphic records is a perfectly normal one; and that the interval, even at its briefest

is long enough to allow the drug to complete the round of the circulation.

Of the symptoms, that which generally precedes is the fall of blood-pressure. This commences as a gradual and steady descent which may last for 5 or 7 seconds without any marked variation in the pulse supervening. Always after that interval, however, and occasionally without any interval, the pulse undergoes a great change. Its rapidity suddenly sinks to less than half its former rate, and it records itself on the revolving cylinder as deep, large curves. The blood-pressure, meanwhile, continues to fall, the gradient of its descent apparently not being altered by the change in pulse. This phase lasts a variable number of seconds, *i. e.* from 10 to 35 seconds, when convulsions or violent muscular movements intervene, and raise the mean blood-pressure suddenly and in an irregular manner. The struggles last for a longer or shorter time; but, as repose is again established, the line of mean pressure is seen to resume its descent, the pulse exhibiting its former abnormal characters, or having become less rapid and feebler. This phase, if the dose be lethal, endures until death; or it may be interrupted by another paroxysm of struggles and afterwards re-appear, to remain until death. If the dose be not lethal, but still have been large enough to induce marked symptoms, the pulse at this stage does not become feebler. The blood-pressure stays its descent, or even reverses its course, and, with many irregular fluctuations due to violent strugglings, tends to its former level. The pulse also resumes its usual characters; and the tracing on the recording cylinder ultimately becomes quite normal.

If the dose be still smaller, the phases are more rapidly passed through. The descent of blood-pressure is of very brief duration, and gives place to a rise, which occasionally leads for a time to a blood-pressure considerably above the usual level. In the course of this rise the heart-beats again become normal.

There is, therefore, to be observed in cases of poisoning by pyro-phosphate of sodium a two-fold change in the circulation, (1) a fall in blood-pressure; and (2) a variation of pulse. The cause or causes of these it will now be necessary to discuss.

In the first place, these symptoms, though they must modify each other, are originally distinct. It might indeed appear that the slow and feeble heart, by driving into the arteries less blood than the latter expel owing to the tension of their walls, was the immediate cause of the diminished blood-pressure; and, unquestionably, any change in such important conditions of the normal blood-pressure as the vigour and rapidity of heart-beat, when once established, must very materially affect that pressure. But that the altered pulse originates the fall in blood-pressure is clearly not the case, since most frequently the latter precedes the former by a few seconds; and, although the two phenomena occasionally *coincided,* no case occurred in which the alteration in heart-beats was observed to come first.

In the second place, we must recall what has already been more fully discussed in another paper, viz. the action of pyro-phosphate of sodium on the muscular tissue of the heart. This action it is important to bear in mind, when it is remembered that the substance of the heart and the chief element in the vascular walls—chief, that is to say, in regard to their tonus—are composed of muscular tissue, change induced in which might possibly be called in to account for the circulatory symptoms. It would appear that pyro-phosphate of sodium is by no means devoid of action on the cardiac muscle, which, when bathed by serous solutions of it invariably fails sooner or later to respond to stimulation. But we doubt if all the effects of those solutions on the beating heart are to be accounted for solely by their action on the muscular tissue. The very curious difference in the action on ventricle and auricle—the former being at once contracted tightly, while the latter is merely slowed—is a point not to be omitted from consideration, as possibly implicating some other agent; while it must not be forgotten that the nervous centres in the spinal cord concerned in the production of movements are undoubtedly acted upon in poisoning by pyro-phosphate of sodium. It seems, therefore, not unreasonable to suppose that the symptoms described are, in part at least, due to lesion of some portion of the nervous system related to the heart and vessels.

With respect to the heart, as is well known, the ordinary

movements are caused by certain intrinsic nerve-centres which distribute rhythmically to the muscles the nervous energy necessary to produce movement. These nerve-centres are further regarded as under the control of other nerves which originate in the cerebro-spinal axis, and which can influence the distribution of that energy so as to quicken or slow, or even stop the cardiac movements. With acceleration we have here nothing to do. Hence the action of pyro-phosphate of sodium on the heart must be effected either through the vagus—the inhibitory nerve—or through the intrinsic motor ganglia. That the vagus centre is in no way affected by the poison it would be rash to assert in the face of observed facts, such as convulsions, paralysis, etc., which compel us to assume the implication of such a large part of the cerebro-spinal centres. But that it is not the chief factor, or even an important factor, is abundantly proved from the experiments of two of us recorded in a previous paper, and from Exps. V. and IV. of this series. The last-mentioned experiment (Exp. IV.) in which the drug was injected after division of the vagi in the neck, shews that the slowing and cessation of the pulse are not due—or not entirely due—to stimulation of the vagus centre: while Exp. V. where the cord was divided in a curarized rabbit prior to injection; taken in conjunction with the other experiments referred to, in which pyro-phosphate of sodium induced its usual symptoms in an atropized frog's heart, exonerate the vagus-endings and the intrinsic inhibitory arrangements connected therewith.

Hence we may believe that, whatever be the changes induced by pyro-phosphate of sodium in virtue of its being a muscular poison, the operation of the salt upon the intrinsic motor ganglia of the heart concurs in producing the cardiac symptoms.

Equally impossible is it, assuming the implication of the vaso-motor centre, to state at present how far the abolition or depression of vascular tonus is determined by peripheral stimulation of the numerous depressor nerves connected with that centre.

We must not omit to point out and emphasize a few interesting facts observed when frogs' hearts, prepared for

Coates' experiment, are treated with poisoned serum,—facts which are of special importance as bringing pyro-phosphate of sodium, as a physiological agent, into relation with pyro-vanadate of soda.

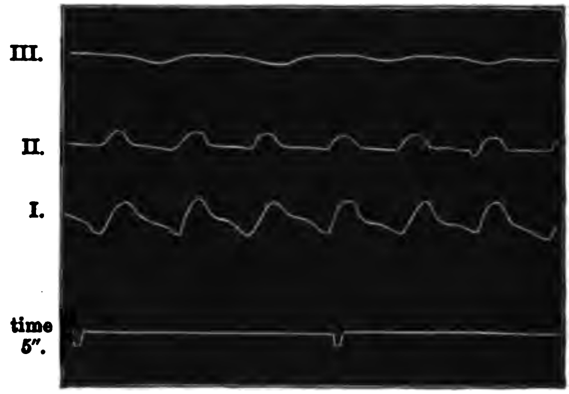
In the first place, the ventricle is instantly firmly contracted, while the auricles are simply slowed.

In the second place, the stoppage of the ventricles in systole occasionally, but very rarely, gives place to a stoppage in diastole, the auricles behaving alike in both cases.

In the third place, stimulation of the vagus-trunk, though powerful enough to stop the slowly-beating auricles, produces no effect whatever on the contracted ventricle.

In the fourth place, thorough atropization of the frog's heart does not at all interfere to prevent the usual action of sodium pyro-phosphate.

The following tracings shew the changes in the character of the heart-beats of a frog's heart prepared by Coates' method, when poisoned by dilute solutions of sodium pyrophosphate.



I. Normal tracing: prior to poisoning.
II. Shortly after poisoning.
III. Some time after poisoning.

OBSERVATIONS ON THE PHYSIOLOGICAL ACTION OF CHROMIUM. By JOHN PRIESTLEY, *Assistant Lecturer in Physiology, The Owens College, Manchester.*

(From the Physiological Laboratory of Owens College.)

I. INTRODUCTION.

WHEN engaged some time ago in investigating the physiological action of vanadium, it appeared of some interest to compare the discovered operation in the body of that metal with the operation of an element to which vanadium was at one time supposed to be closely allied, viz., chromium; for although Roscoe had established the true relationships of vanadium as a pentad metal, yet the proximity, amounting almost to identity, of the atomic weights of vanadium and chromium (V. 51·2, Cr. 52·2) rendered such a comparison of some moment in this era of bold toxicological speculation. On a search being made, however, it appeared that the exact effects of exhibiting chromium in the animal system were still unknown. The rough toxicology had certainly been learnt in the manner in which, unfortunately, much of our toxicological knowledge has come to us, viz., from cases of accidental poisoning of workmen and others. Knowledge so obtained is seldom in a comparable form; hence it became necessary, in the case of chromium, to supplement it by a systematic investigation.

This was undertaken, and the results, which I have had by me for upwards of two years, are now for the first time made public.

The exact state of our knowledge of chromium poisoning in 1874, is thus summed up by Hermann (*Experimentelle Toxicologie*): "Die Chromsalze und Chromalaune haben nach den spärlichen "darüber vorliegenden Erfahrungen ähnliche Wirkungen wie die "Aluminiumsalze.—Die Chrom-Säure ebenso, aber schwächer, das "Kaliumbichromat, auch das neutrale Kalichromat, wirkt heftiger "erbrechen- und durchfall-erregend als andere neutrale Alkalisalze. "Experimentelle Untersuchungen über diese Körper sind fast noch "gar nicht angestellt." Since then I am not aware that any contributions have been added to our knowledge of the physiological action of these bodies except a series of observations published in the last

number[1] of the *Archiv für experimentelle Pathologie und Pharmacologie* and entitled "Beobachtungen über die toxische Wirkung der Chromsäure," by Dr E. Gergens, Assistent am Physiologischen Institut zu Strassburg. It contains the details of some half-dozen experiments chiefly performed upon dogs which had had their spinal cords divided at the level of the 12th dorsal vertebra. The remarkable roughness of most of the experiments, in which the poison was introduced by puncturing the cord itself with a Pravaz syringe inserted through an aperture previously made from behind, render it impossible to attach importance to Dr Gergens' conclusions; while the paucity of the experiments alone, without considering their contradictory results, attest the crudity of the theory of action he seeks to set up. One very important result of his investigation, however, must not be lost sight of. The perfect concurrence of all his experiments proves that albuminuria, with cloudiness of renal epithelium, urinary casts and congestion of the kidneys, are concomitants of poisoning by chromic acid and neutral potassium chromate; while his control-experiments sufficiently indicate that they are referable to the drug, and not to the injuries due to the method of injection. I have brought these facts into relation with the results of my own observation, inserting them, with due acknowledgment, in their proper place in the text.

It now only remains to be mentioned that the salt used in this research was the neutral chromate of sodium (Na_2CrO_4) —to avoid any decided acid or alkaline reaction, and to secure an inert base, being specially kept in view.

It has not been deemed necessary to print a large number of protocols: those which are given may be regarded as typical cases.

II. Notes of Experiments.

Exp. I. Rabbit, wt. 1301 grm., dose 4 cc. of a solution of neutral sodium chromate containing 5 p.c. CrO_3, injected underneath the skin of the back. Within 15 min. of the time of injection symptoms of poisoning set in. The head was thrown back in jerks; the hind limbs seemed paraplegic. The animal became weak and lay over on its side or back. Within 48 min. of injection the corneæ became insensitive, though pinches applied to the skin of the limbs were then felt and responded to; and in 1 min. more—49 min. after injection—the animal died with asphyxial symptoms, with head thrown back and legs outstretched.

Exp. II. Guinea-pig, wt. 422 grms., dose 1 cc. of solution of neutral chromate of soda containing 10 p.c. CrO_3, injected under the skin. Within 16 min. of the time of injection symptoms of poisoning appeared. The animal became very quiet, and would not stir when

[1] July, 1876.

pushed. When, some minutes afterwards, it moved spontaneously into a dark corner, it was with difficulty, owing to a tendency to fall over on the left side. Its breathing at the same time became spasmodic. On lying down on its right side it was seized first with spasms of head and limbs, and then with severe retching. The strong spasms subsided into slighter twitches affecting the muscles of the posterior limbs and back; and, as the animal moved, its hind legs were imperfectly controlled. The retching seemed to involve the whole of the muscles, but especially those of the hind legs. 35 min. after poisoning paralysis of the posterior half of the body was well advanced, to run or to stand being impossible. Respiration came at longer and longer intervals and in painful gasps. After a final severe trial to vomit, which left the abdominal muscles strongly contracted, the animal rapidly sank; and within 40 min. of the time of injection it died.

Sectio cadaveris disclosed the following:

1. Presence of much greenish-yellow coloration in the cellular tissue punctured by the injecting syringe.

2. Congestion of alimentary tract.

The *stomach* contained a light grey thin grumous mass. It exhibited much congestion, at the back and cardiac end, of a cherry colour. Ecchymoses appeared externally and internally on the walls. Arborescent injection of chocolate-coloured blood was noticed at the pyloric end externally (the peritoneum being *in situ*).

The *duodenum* exhibited cherry-coloured congestion of mucous membrane, chiefly, but not solely, at its free border. Externally, like the stomach, it appeared much injected with chocolate-coloured blood.

The *rest of the small intestine* exhibited the same characters of congestion, but to a slighter degree. It was filled with the same gruel-like contents as the stomach.

The *large intestine* was slightly congested.

3. Partial brown congestion of lungs, viz. at the top of the right lung, and a few surface patches elsewhere.

4. The liver was deeply cherry-coloured and equally coloured throughout its mass.

5. The kidneys were somewhat congested with cherry-coloured blood.

6. The auricles were contracting. The blood, which was of a deep chocolate colour, coagulated normally. The blood of another guinea-pig, similarly poisoned, exhibited absorption-bands resembling those of methæmoglobin when examined by means of a Browning's microspectroscope.

EXP. III. Small frog. Dose, 1·5 cc. of solution of neutral sodium chromate, containing 10 per cent. $Cr O_3$ injected under the skin of the back.

Within 10 minutes of injection tremors of the thigh-muscles were noted. Respiration had already ceased, and the cornea was insensitive. The fore limbs were very firmly folded. Reflex action was slight, and the efforts of the frog, when laid on its back, to regain the upright position were slight, short, and ineffectual.

Fifteen minutes after injection the strongest acetic acid applied to the skin of the foot only induced slight movements; but on my trying to open his firmly-shut mouth the frog extended his hind legs once violently. This peculiar movement, not calculated at all to avoid or repel the irritant, was several times repeated, viz. once when I pinched the skin of the folded arms, again on each of two occasions when I tapped on the top of the head, and a fourth time when I turned the frog on to his back. Shortly after, about 25 minutes from the time of injection, some power of reflex movement seemed to have returned, as was evidenced on pinching the toes. All this time the before-mentioned quivering of the thigh muscles continued.

When 55 minutes had elapsed since poisoning, as reflex action was entirely abolished, the frog was opened. The heart had stopped in diastole and was filled with dark chocolate-coloured blood. The muscles were of a yellowish-brown colour. Free exudation into the cavities of the body had occurred. On testing with interrupted induced currents, the muscles, nerves and cord (as far as it is a conductor of impressions) were found to be sensibly normal.

Exp. IV. Small frog. Dose, ·25 cc. of solution of neutral sodium chromate, containing 10 per cent. CrO_3, injected under skin of back.

The right femoral artery was tied to prevent the passage of the poison to the tissues of the right leg.

Within 15 minutes of injection the arms became vigorously and continuously contracted. Respiration was slight and the cornea well-nigh insensitive. On laying the frog on his back both legs were tetanically stretched for a few seconds. The legs, which remained spread out after their tetanic extension had passed over, were not, as usual, retracted to the body when the toes were pinched, but both, on the contrary, were again forcibly stretched out.

Within 35 minutes of administering the poison the power of reflex action was entirely lost; the cornea was insensitive; but the arms still remained firmly contracted across the chest. On opening the frog the heart was found to be stopped in diastole; but it responded to stimulation, viz. on pinching with forceps.

The muscles were yellowish-brown in colour. There had been extensive exudation into the various cavities of the body. On testing with electrical stimuli, viz. interrupted induction-shocks, the poisoned and the non-poisoned muscles and nerves shewed themselves equally normal. The cord also was sensibly uninjured as far as its conducting properties were concerned.

Exp. V. July 21, 1874. Rabbit, weight 1760 grms., dose 6 cc. of a solution of neutral sodium chromate, containing 5 per cent. CrO_3 in two equal parts, injected into right external jugular vein.

Time.	Pulse in 10 sec.	B. P.	Remarks.
H.M.S.			Kymographic cannula in left carotid.
3.31	46	182	Respiration curves 11½ in 10 sec.
3.33			Struggles.
3.34·30		178	
3.35			Two or three violent struggles.
3.37			Resp. curves very marked. Pulse very marked.
3.41.30	39	184	Resp. curves occasionally shewn.
3.41.35	41	182	Injection of 1st quantity commenced.
3.41.45	38½	190	Resp. curves slight.
3.42.15	41	192	Pulse quite normal.
3.43	43	196	Resp. curves have ceased.
3.43.10			B. P. begins to fall. Pulse 41 during preceding 10 sec. and 43 during succeeding 10 sec., during which it is feebler.
3.43.20		161	B. P. ceases to fall. Injection complete. Struggles then occur which raise the B. P. to 188. Pulse vigorous. Resp. curves exceedingly well marked for 15 sec.
3.43.40	37	188	Resp. curves become imperceptible: pulse becomes feebler. B. P. falls to 160.
3.44	46		Struggles then occur, whereafter resp. curves again
3.44.5		160	become visible, and the pulse regains its vigour.
3.44.30	37	144	B. P. now slowly falls.
3.46	42	112	Resp. curves still well marked: pulse very vigorous.
3.48			Respirations 7 in 10 sec.
			Resp. curves 8 in 10 sec.
3.49.30	45	98	Respirations 12 in 10 sec.
			Resp. curves 11—12 in 10 sec., tolerably well marked.
3.54.15			Violent struggles which send up the B. P. to 164.
3.55	45	164	Resp. curves 12 in 10 sec.
3.55.30	45		Struggles; B. P. irregular.
3.56 to 3.57	43	180	Quivering convulsions of extremities. B. P. very irregular. Eye sensitive. Resp. curves well shewn.
3.58	41	172	Blood noticed to be very dark. Resp. curves well shewn (10—11 in 10 sec.). Pulse well marked.
3.58.30			B. P. irregular.
3.58.40			Respirations 10—11 in 10 sec. and deep.
4.	40	135	B. P. has fallen; struggles ceased. Resp. curves well marked.
4.3.10	41	78	B. P. gradually fallen. Respirations 7 in 10 sec. Resp. curves 7 in 10 sec. Pulse vigorous.
4.4.20	42	99	B. P. steadily rises. Pulse and resp. curves as before.
4.4.50		72	B. P. falls steadily. Pulse and resp. curves as before.
4.5.40	40	82	B. P. rises steadily. Pulse and resp. curves as before.
4.7	40	79	Pulse and resp. curves just as before.

Experiment V. *continued.*

Time.	Pulse in 10 sec.	B. P.	Remarks.
4.13	22—23	70	Characters of pulse entirely change: now we have long, full beats, large excursions of the pen, a second beat often following before the diastole of the preceding has run its usual course. (See Fig. 2.)
4.13.40		78	No respiration curves.
4.14			Blood looks almost black.
4.15	19	80	More of the double beats here noticed.
4.17	19	82	As before.
4.17.40			The dicrotism here occasionally seems to resolve itself into two perfect pulsations. B. P. rises.
4.18			The above is now more frequently the case. B. P. rising.
4.18.25	32	104	
4.25	27	84	Pulse regular and vigorous; no resp. curves: now and then diastole seems to elongate, giving a characteristic appearance as of "slipping" a beat. (Fig. 3.)
4.34.30	31	87	Pulse seems quite normal.
4.41.30	31	93	Resp. curves well shewn.
4.52.50	32	98	
5.17	31	127	B. P. has steadily risen.
5.17.10	31	127	INJECTION of second quantity COMMENCED.
5.18	30	138	
5.18.10			Struggle making B. P. irregular.
5.18.25		156	Injection continues. Irregularities of B. P. due to struggles.
5.18.35	30	148	B. P. Pulse and resp. curves quite regular and vigorous.
5.18.50	27	164	Pulse has become large, and exhibits the tendency to "slip" above noticed.
5.19.20 to 5.19.50	26 to 22	146 to 187	B. P. irregular. Injection complete. Cries of rabbit. Pulse large and irregular. No resp. curves.
5.20.40	23—24	157	B. P. regular; pulse large and regular. Resp. curves regular.
5.21.20	23	114	B. P. falls suddenly.
5.24	24	58	Steady fall of B. P. Pulse full and large; left eye insensitive; right somewhat insensitive. Resp. curves long and not always to be seen.
		50	Quivering of fore part of body. B. P. quite steady.
5.25.10	23	48	Struggles of whole body without any alteration of B. P. whatever: pulse seems to cease entirely.
5.26	23	46	Stretching out of hind limbs. Pulse feebler.
5.27			No respiratory movements. Pulse very feeble, long, and hardly to be counted.
5.27.30	19	38	
5.30			Dead.

Exp. VI. Rabbit; weight 2160 grms., dose 2 cc. of a solution of neutral sodium chromate, containing ·10 per cent. CrO_3, injected into vein (external jugular).

Time.	Pulse in 10 sec.	B. P.	Remarks.
H. M. S.			Kymograph at carotid.
1.16	43	208	Normals. Resp. curves 8 in 10 sec.
1.17		208	Right vagus divided.
1.17.10	45	202	
1.17.15		216	Left vagus divided.
1.17.40	46	220	
1.19	48	224	No respiration curves.
1.20.30	47	224	Injection commenced. } No resp. curves.
1.21.11	46	226	
1.21.31			Injection complete.
1.22	49	250	
1.25	51—53	147	B. P. has gradually fallen. Struggles followed immediately after completion of injection; but none occurred afterwards to disturb the gradual fall of B. P.
1.29.30	44	184	Pulse quite normal. Since 1 h. 25 m. there have been occasional struggles which send up the B. P. temporarily and suddenly.
	36	176	
1.37.20	38	72	Resp. curves 7 in 10 sec.
1.39	36	52	Pulse firm. Regular fall of B. P, not disturbed by struggle. Resp. curves 4 in 10 sec. Respirations were 5 in 10 sec., by direct counting, a little time previously.
1.40.30	34	44	Pulse feebler. Resp. curves slight, 4 in 10 sec.
1.42			A series of struggles begin which disturb the B. P.
1.43.30			Struggles continue, rapidly following one another.
1.45			Convulsive movements of thorax at every respiration.
1.48	34	36	Respiration ceasing. Resp. curves not to be seen. The B. P. sank gradually; the pulse weakened and
about 1.51			lengthened until the rabbit died about three minutes after.

The following figures illustrate the action of neutral sodium chromate on the blood-pressure and pulse. (The straight lines at the bottom of each figure is the line of no-pressure; the curved line is the tracing of the kymographic pen; the intermediate interrupted line, where it exists, indicates intervals of 10 seconds. The tracings are *not* reduced in size.)

Rabbit—1760 grms., dose (1) 3 cc., (2) 3 cc., solution neutral sodium chromate containing 5 per cent. CrO_3 injected into veins. See Exp. V.

Fig. 1. Normal.

Fig. 2. Tracing taken 32m. after injecting 1st dose.

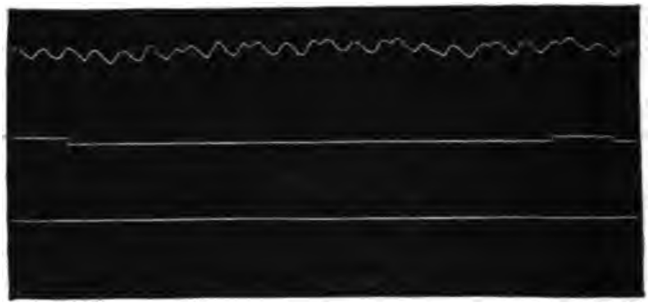
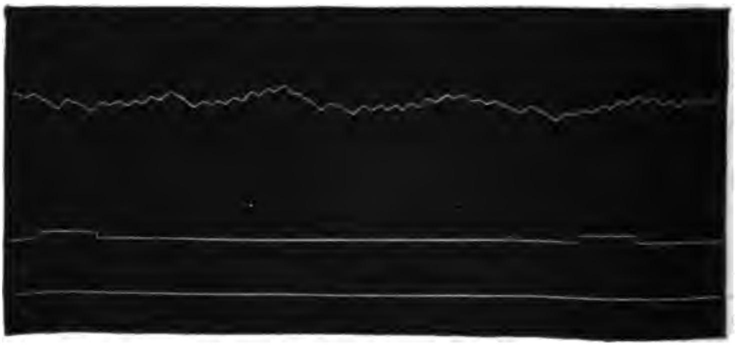


Fig 3. Tracing taken 44m. after injecting 1st dose.



Rabbit—1400. Dose 3 cc. of solution neutral sodium chromate containing 5 per cent. CrO_3, injected into veins.

Fig. 4. Normal, just prior to injection.

Fig. 5. Tracing taken 13 m. 10 secs. after injection.

Fig. 6. Tracing taken 17 m. 45 secs. after injection.

Fig. 7. Tracing about 24m. after injection. The 'slips' here were synchronous with respiration.

Rabbit. Dose 1 cc. 1 cc. 1 cc. } neutral sodium chromate solution, containing 5 per cent. CrO_3, injected into vein.

Fig. 8. Normal.

Fig. 9. Tracing taken 55m. after 1st injection, 33m. 15 secs. after 2nd injection, 7m. 30 secs. after 3rd injection.

Fig. 10. Tracing taken 4m. 30 secs. after the last tracing.

Rabbit[1]. 2085 grms. Dose 3 cc. (nearly) of solution of neutral chromate of sodium, containing 10 per cent. CrO_3, injected into vein. Rabbit very violent.

Fig. 11. Normal.

Fig. 12. During injection. Usually the rise after injection was not so marked as in this case.

[1] This rabbit had lost much blood.

Fig. 13. Tracing taken 40 secs. after injection. Violent struggles were taking place.

III. RÉSUMÉ.

In brief, the symptoms of acute poisoning by chromates are as follows:

·1 to ·3 gr. $Cr\,O_3$ in the form of neutral chromate of soda is a powerful poison for rabbits and guinea-pigs, producing death in from 4 min. to 30 min. (according to the vigour of the animals) if injected at once into veins; and in from 40 min. to 50 min. when introduced beneath the skin. ·15 grm. $Cr\,O_3$ in the above form, when injected into a vein in three equal doses at intervals of 23 or 24 minutes, killed in 1 h. 10 m.; while ·3 grms. $Cr\,O_3$ in two equal doses in the case of another rabbit took 1 h. 50 m. to cause death.

Death is preceded by spasms or convulsions, and violent retching, which commence a few minutes after the injection of the poison. In frogs muscular tremors, tetanic contraction of the pectoral muscles and the flexors of the fore-limbs, and tetanic extension of the hind-limbs on the application of slight stimuli, represent this class of symptoms. Convulsions are varied, or succeeded by paralysis of motion in mammals, and in frogs, as is usual, of respiration also. In frogs, too, the power of reflex action is speedily abolished.

The blood-pressure generally[1] rises within 10 sec. of injection of

[1] In one case only it failed to rise appreciably.

the poison into the jugular vein; but this rise speedily gives way to a fall, which begins from $\frac{3}{4}$ of a min. to 3 min. after injection. A downward tendency is steadily maintained until death; previous to which the blood-pressure becomes extremely slight; and it is only interrupted by occasional struggles with their consequent irregularities of vascular tension. Meanwhile the pulse preserves a strict normality, save that, as the blood-pressure falls it becomes somewhat deeper—a circumstance due presumably to the larger excursion of the laxer arterial walls. With this exception it appears to be quite independent of the blood-pressure, maintaining its rapidity until the latter has reached a mean equal to one-half, or one-third, of the normal. Afterward, however, a peculiar modification begins to occur at irregular intervals; and continues to appear for longer or shorter periods. After a time it gives place to a pulse of normal character, but of less than the original rapidity. Again it returns; but it invariably disappears just before death, when the pulse gradually lengthens and weakens. This phenomenon gives one the impression of the heart stopping suddenly for the space of a beat, again setting up normal pulsation immediately afterward,—as it were, 'slipping' a beat. That is to say, the blood-pressure merely continues the fall which it had initiated during the preceding diastole, and the impression gathered from the graphic record is one of prolonged dilatation of the ventricle. These slips may occur coincidently with struggles; but generally this is not the case (Figs. 1—10). On one occasion, for a space of nearly two minutes, towards the close of an experiment, they continued synchronous with inspiration. Generally they are less regular, occurring after every 8 to 3 ordinary heart-beats; and sometimes they are so lawless as to give the tracing an appearance like that of Fig. 13. They are interjected into the series of ordinary heart-beats without previous warning; and they do not seem to specially, or at once, affect the mean blood-pressure.

After these irregularities have set in, although the pulse may again become normal in appearance, it never regains its previous rapidity, but remains deep and slow.

The variations of blood-pressure, coincident with respiration, disappeared and reappeared several times after the injection of chromate of sodium into the veins; to which no importance can be attached, since they are frequently noticed to do the same in rabbits which have not been poisoned.

The *post mortem* examination of the animals experimented on disclosed the following.

The reduction of the drug in the cellular tissues at the point of injection beneath the skin, as evidenced by the yellowish green colouration.

Free exudation of fluids, in the case of frogs, into the various cavities and spaces of the body. The muscles also in frogs were of a yellow-brown colour—the colour of the original solution, and not due therefore to any reduction.

Congestion and ecchymoses of all parts of the alimentary canal

below the cardiac orifice of the stomach. Semifluid grumous intestinal contents.

Congestion of lung in the case of a guinea-pig. (It should be noted that guinea-pigs readily become afflicted with lung diseases.)

Congestion of the kidney. Dr E. Gergens has also noticed, in dogs and rabbits, cloudiness of the epithelium, urinary casts, and albuminuria, to follow poisoning by chromic acid and neutral potassium chromate.

Stoppage of the heart in diastole, even in frogs. The frog-heart, so stopped, responded but languidly to the stimulus of pinching. Chocolate colouration of the blood which exhibited the bands of methæmoglobin when examined through a spectroscope.

Muscles, and nerve-trunks and extremities, appeared to be sensibly normal.

Of these symptoms, with the exception of the variations of blood-pressure and pulse, the interpretation seems so obvious as not to need comment. Indeed even the immediate cause of the disturbance of blood-pressure can readily be seen in the face of the facts disclosed. The evident normality of pulse which continues long after the fall has become marked, at once excludes the possibility of a cardiac origin of the fall in blood-pressure. Moreover, it renders it extremely improbable that the fall was produced by a dilatation of the vessels in consequence of a direct action of the drug upon their muscular walls; for it is hardly possible that a drug should at the same moment cause rapid death of one set of involuntary muscles, viz. those of the arteries; and leave another—those of the heart—to which access is equally free, apparently uninjured. To disturbance of the vaso-motor centre, therefore, we must turn for an explanation of the varying blood-pressure. The above considerations, of course, do not exhaust the discussion of the subject; but the sustained nature of the fall of pressure makes any reference of it to a reflex origin, through excitation of depressor nerves, in the highest degree improbable; while the general aspect of the tracings obtained, and the certain knowledge that other centres in the cord, as the motor centres, are affected by the poison, place the matter beyond a reasonable doubt.

The cause of the pulse-change is not so apparent. It is, however, clear that the peculiar slips, the nature of which is far better gathered from the accompanying figures than from a description, are due to a temporary continuance of the ventricular diastole. This, I think, will be granted on a comparison with similar tracings taken from a heart stopping after stimulation of vagus.

Now prolonged diastole of ventricle may occur in consequence of one or more of three causes:

(1) Stimulation of vagus in some part of its course.

(2) Stimulation of the hypothetic inhibitory mechanism, intermediate between vagus and motor centres.

(3) Failure of muscular action due to some change in muscle-substance itself.

Of these the third may be briefly dismissed. The *formal* regularity of the pulse to the very close of life, with the exception of the

occasional slips; and the fact that the latter occur suddenly and often singly in the midst of series of regular beats; seem to eliminate from the question, as before remarked, all suspicion of muscular poisoning. The decision between the remaining possible causes is speedily made; for a reference to Exp. VI. performed on a rabbit whose vagi were previously divided, will shew that the characteristic phenomenon did not once occur. To this circumstance the fullest importance must be given; since in no case out of six experiments made on rabbits with vagi intact were the symptoms wanting. This experiment, which was confirmed by repetition, at once eliminates the second possible cause and establishes the first. Stimulation of the cardiac inhibitory portion of the vagus at some point above the level of section, *i. e.* above the middle of the neck, must, with the facts at present before us, be regarded as the efficient cause of the variations in the character of the pulse: and the preservation of the conducting powers of motor nerves during acute chromium poisoning, leaves us no alternative to considering the centre of the vagus in the medulla as the exact point of lesion.

IV. CONCLUSION.

As is the case with many other irritant metallic poisons, the action of chromium salts on the animal economy may be regarded as twofold, viz. an action on mucous membranes, and an action on the great nervous centres.

Of the former the evidence rests chiefly upon *post mortem* appearances. The congestion and the hæmorrhagic infarctions discovered in the internal coat of stomach, and small and large intestine, and which so rapidly follow injection of the drug; the character of the contents of the intestines, which consist of copious fluid, or but slightly viscid, grumous material, sufficiently indicate the nature of the changes which seize upon the mucous membrane of the alimentary canal: while the congestion of kidney, the cloudiness and fatty degeneration of its epithelium (Gergens), together with the occurrence of albuminuria (Gergens) with casts, shew at once the implication of the renal secreting apparatus.

As evidence of the second action of chromate-salts there are the various phenomena which have been already noticed in detail, (1) of stimulation, and (2) of depression, of various cerebro-spinal centres. Of these, as one of the most important, the vaso motor centre must be mentioned. This centre is somewhat stimulated as soon as the poison has had time to circulate to the brain, the arterial tonus being considerably

raised shortly after venous injection; but, after a brief period of exaltation, the power of the centre gradually declines; it loses its hold on the vessels, which, as death approaches, are apparently dilated to the full.

The respiratory centre in mammals would appear not to be materially injured, at least the methods of observation adopted have not been adequate to shew any abnormality; but in the frog, as may frequently be noticed in the cases of paralysis otherwise induced, the movements of respiration are the first to cease—a fact which the persisting vitality of nerve-trunks compels us to attribute to functional death of the respiratory centre.

The cardiac-inhibitory centre in the cord must also be regarded as acted upon in an irregular manner by chromate of soda, if, as I have sought to shew, the curious variations in the pulse-tracing which constantly follow poisoning by this salt are really referable to inhibition.

The motor centres of the cerebro-spinal system are manifestly acted upon. The convulsions in guinea-pigs and rabbits, followed by paralysis, chiefly but not solely of the lower extremities, and the tetanic contraction of the arms in frogs, cannot be due to any other cause. The abolition of reflex action in frogs is an analogous case, and shews that the centres concerned in the origination of motor impressions in accordance with afferent or sensory stimuli are also affected by this poison; for the abolition was due to injury neither of motor nor of sensory nerve-trunks or terminals, and must therefore have been caused by lesion of the reflecting centres.

With regard to the heart, I do not think we can attribute to chromium any direct or special action upon it. The introduction of a comparatively large amount of the strong solution of any salt into the blood must necessarily so disturb the coarser, physical characters of that fluid, as to cause it to react upon the tissues it bathes in a manner injurious to their function; but this is not, rightly speaking, a special action of the salt. In this sense only can it be said that chromate of soda affects the heart, and causes, for example, that stoppage in diastole which must be regarded as very remarkable when occurring in the frog.

It is intended, however, to enter more fully into this matter in a subsequent research.

CASE OF UNIVENTRICULAR OR TRICŒLIAN HEART[1].

By ROBERT ELLIOT, M.D. (*Edin.*), F.R.C.P. (*Lond.*) *Carlisle.*

THE case of J. C——, a clerk in an office, most nearly approximates to the 17th in Dr Peacock's elaborate work, 2nd Edit., p. 148; and to the 4th published by Dr Cockle in the *Med-Chir. Trans.*, Vol. XLVI. p. 200, quoted from Mr King in Vol. IV. of the *Monthly Journal of Medical Sciences.*

The peculiarity of J. C.'s case consisted in the combination of transposition of the great vessels; smallness of the aorta, and large size of the pulmonary artery; total absence of ventricular septum; all but total freedom from pericardial adhesion; equally healthy and efficient lungs; the attainment of the age of 19 years and 8 months; and lastly, amiability and good humour.

Cyanotic signs were first observed at 3 months of age, and gradually increased as he grew older. The livid complexion, the clubbed finger ends, the sensibility to cold, the inaptitude for bodily exertion, the stuffy breathing, the high intelligence, were such as are usual in cyanosis. He was short and slight in figure, had no beard, his chest was small, rounded and projecting, especially at the left border of the sternum, and with trifling movement. On percussion of the chest there was dulness in the precordial region far beyond normal limits. The heart's action was nervous and thumping, with a whizzing bruit occasionally accompanying the systolic sound, the 1st and 2nd sounds, however, were otherwise normal. His pulse was an exceedingly shabby one, and strangely variable in force, but always about 80. There was no other indication of valvular defect, nor any sign of pericardiac disease.

Appetite good, bowels regular, urine generally turbid, sleep of average length and depth, but with thick stuffy breath-

[1] Read to *Med-Chir. Soc.* London, June 23, 1868. Abstract in *Proceedings* of that date.

ing. In summer, especially in warm weather, feels himself best. His health was wonderfully good and uniform.

In his last and only important illness, extending over three weeks, his appetite was extremely poor, he vomited frequently, his tongue was dirty, aphthous, and sore; and his pulse was small and rapid; he had much precordial pain and oppression, his breathing was laborious, so that he was obliged constantly to sit up, he had drowsiness gradually deepening, extremities slightly œdematous, very cold and livid, face still more livid, and mouth and tongue most so. He died calmly, and as if through gradual exhaustion, on May 19th, 1867. He got great relief from the inhalation of oxygen, but was not troubled with any other medication. Under the influence of this gas his precordial pain lessened, his colour mightily improved, his bowels, skin, and kidneys, all acted better, and he breathed so much more freely, that he said he had not felt so easy and well for years.

An autopsy was made 2½ days afterwards. There was great œdema of the extremities, the body was livid, especially the extremities, the neck and face more so, and the inside of the mouth most so, as in life.

The brain was not inspected.

The lungs were quite healthy in appearance, no trace of tubercle or of any disease either on or in the lungs, both equally normal. Slight effusion existed in each pleural sac. No adhesions.

The liver was healthy.

The pericardium externally was normal, internally there was slight effusion, and but a single adhesion, trifling, old, and elongated.

Examination of the heart, July 24th, 1867, after rather over two months immersion in spirit; present Drs Embleton and Elliot.

Exterior: The organ appears large, measures round its widest part 11¼ inches, and in length 4½. The bulk was chiefly due to the right or pulmonic heart which was distended with grumous blood. External surface healthy, except the old adhesion above-named, on the front near the apex. On placing the heart with its anterior surface upwards, the anterior longi-

tudinal furrow with its vessels holds the usual position, ending above and to the right side of the apex.

The aorta and pulmonary artery are seen to be reversed in position, from the right side of the heart springs the aorta, having on each side of its origin the right and left auricular appendages. The aorta is not more than half an inch in diameter, its arch is formed as usual, and the customary three branches are given off from it. All three are small, in proportion to the size of the trunk from which they arise; the innominata bifurcates within half an inch of its origin. Immediately behind the origin of the aorta is placed that of the pulmonary artery, which measures an inch and three quarters in diameter at its commencement, passes up behind the ascending part of the aorta, and bifurcates as usual under its arch; and just below its bifurcation its diameter is 2 inches. The ductus arteriosus is quite closed. The right auricle and the right side of the ventricular part of the heart appear unduly large; this auricle is a good deal larger, both as to its sinus and its appendage, than the left.

The venæ cavæ enter the right auricle normally, and the usual four pulmonary veins are normally connected with the left auricle.

Interior: The ventricular division of the heart is one large cavity, no trace of septum is visible, the organ having been freely opened from the apex towards the base. The reticulations of the columnæ carneæ on the right side are not nearly so numerous and complicated as those on the left side; the musculi papillares are nearly as large on the right as on the left side, and the ventricular wall on the right is very nearly as thick as that on the left side.

The aortic aperture is placed in the normal position of that of the pulmonary artery, and the latter in that of the former; the orifice of the aorta is small, like the vessel itself above, its valves are of the usual form, and healthy in appearance.

The pulmonary orifice is somewhat constricted, contrasting thus with the wide calibre of the trunk above, and yet it has about twice the diameter of the aortic opening, the latter admits easily a fore-finger, whilst the former will accommodate two fingers.

The valves of the pulmonary artery are thickened, particularly at their borders, but unequally so, the anterior and the right posterior segments being much more so than the left posterior, which is not only thinner but also a little smaller than the others. Together, however, these valves appear to be competent to close the opening. The thickened edges of these valves scarcely appear capable of giving rise to the occasional whizzing sound which, during life, accompanied the ventricular systole.

On close examination, just under the right posterior segment of the pulmonary valve, is seen a little bag of membrane, valve-like, convex and bulging towards the pulmonary aperture, concave towards the right auriculo-ventricular opening, and having two or three chordæ tendineæ attached to its otherwise free border. Its exact position was between the last-mentioned segment of the pulmonary valve and the left segment of the tricuspid valve, and might assist that segment in preventing the direct passage of blood from the right auriculo-ventricular aperture to that of the pulmonary artery, but when distended with blood it would be carried somewhat over the pulmonary orifice, and thus, in all probability, give rise to the occasional whizzing above mentioned. This little valvular bag lies in the uppermost part of the space, that is left vacant by the absence of the interventricular septum, and its attached border is fixed between the right auriculo-ventricular aperture and that of the pulmonary artery. A little below this bag, and further back, against the posterior wall of the general ventricular cavity, are seen the adjacent segments of the tricuspid and bicuspid valves connected together, a small papillary muscle running up along a part of their line of union. These two sets of valves appear to be otherwise normally arranged as regards their segments. The right auricle is a good deal dilated, and its walls hypertrophied, the appendage is unusually capacious, and the musculi pectinati strong.

The vestige of the Eustachian valve is visible. The valve of the coronary vein shews a perforation. At the upper and back part of the fossa ovalis exists a rather oblique opening which would admit an ordinarily sized goose-quill. This is the only communication between the auricles, and could not be the

cause of the whizzing murmur. Nothing abnormal in the left auricle.

For other cases of Malformation of Heart, see *Reports of Proceedings of Northumberland and Durham Med. Soc. Session* 1862-63, and ditto 1850, 1st by Dr Embleton and 2nd by Mr Wallis, South Shields, and again, 1858, in ditto, by Mr Bolton. Also, Dr Peacock's work on "Malformations, &c. of the Human Heart," *Brit. Med. Journ.*, Sept. 28, 1872, p. 351, a case by James Johnson, M.B. of Birmingham, (Deficiency, not absence of sept. ventricul.), and the same *Journ.* for Jan. 11th, 1873 a "Case of Tricœlious Heart in which sept. ventricul. was absent, with figs. of exterior and interior," by S. M. Bradley, F.R.C.S. of Manchester.

ON THE CHANGES IN THE CIRCULATION WHICH ARE INDUCED WHEN THE BLOOD IS EXPELLED FROM THE LIMBS BY ESMARCH'S METHOD. By

H. G. BROOKE, B.A. (*London*), and E. O. HOPWOOD, B.A. *Christ's Church, Oxford, Platt Exhibitioners in the Physiological Laboratory of Owens College, Manchester.*

(*From the Physiological Laboratory of Owens College.*)

AN idea suggested itself some time ago to Dr Gamgee that it would be interesting to observe from a physiological point of view the effects produced on the circulation by the application of Esmarch's bandages, and he therefore seized the opportunity of the presence in Manchester of Dr Paul Albrecht, late Assistant in Professor Esmarch's Clinique at Kiel, to commence a series of experiments, which we have carried on, and the results of which are here recorded.

1. Description of method of experimenting.

Our method of procedure is as follows. A strong 3 inch web elastic bandage is taken, stretched tightly under the foot of the individual to be operated upon, and over the ends of the toes, turned and wound upwards in spirals, *lege artis*, passing over a pad placed under the popliteal space in order to make more complete pressure on the subjacent vessels, and then over the thigh. At the top of the thigh two or three overlying turns are made, and the bandage is fastened by means of an ordinary safety-pin, a plan which we found to be as efficient as the use of any tourniquet, and much less painful; throughout the series of experiments we tried to avoid all actual pain in order to eliminate, as much as possible, the influence of any psychical or reflex vaso-motor effect on the pulse-rate, and we succeeded so far as to produce nothing more than a mere feeling of discomfort from the compression which the bandage necessarily exerts.

In order to see if the object has been accomplished, the bandage is removed from the foot upwards with the exception of the few folds, which serve as a tourniquet. If the bandage has been well applied the limb appears perfectly blanched, and after a period of slight hyperæsthesia (in some cases), followed

by paralysis of both motor and sensory nerves, it becomes quite cold and cadaverous. Tapping on the foot then produces the sensation of a series of shocks on the section of the thigh immediately above the 'tourniquet.' The subject was in each case stripped and in the recumbent posture, and the experiments were made an hour or two after a meal. The normal pulse-rate and sphygmographic tracings (at three different pressures) were first taken, the bandage was then applied as described, the pulse-rate being now, as indeed throughout the whole experiment, carefully and constantly counted.

On the completion of the bandaging three more tracings were taken by the sphygmograph, which was kept continuously applied to the arm. The second leg was afterwards treated in the same manner, and, after an interval, the two bandages simultaneously released, the pulse being now most carefully counted for short periods, and the observations continued until the reestablishment of the normal condition. On releasing the bandages the blood is seen to rush quickly down the leg, causing an intense blush, and, without any uncomfortable sensations, the limb in a few moments completely regains its power.

Throughout the experiments the following observations on the general conditions of the persons experimented on were made. In addition to the local alterations in sensibility, it was observed that usually some time after the bandages had been applied the individual complained of a great fulness of the eyes, accompanied sometimes by a throbbing of the iliacs and of the common carotids. After the blood had been allowed to re-enter the limbs intense shivering, sometimes almost amounting to rigor, but unaccompanied by any sensation of cold, was observed.

Five individuals, all vigorous adult males, varying between the age of 21 and 27 were experimented upon. Three of them were experimented upon on two different occasions, so that altogether eight sets of observations were made. These led to the most concordant results, which we shall proceed to state before quoting the actual data of some of the experiments.

General results of the Experiments.

1st. Whilst one lower limb is being bandaged an increase in the pulse-rate always occurs, which may continue for some

minutes, but which more commonly falls quickly to about the normal rate. 2nd. During the bandaging of the second lower limb the pulse again becomes quicker, but the quickening is only temporary; when the pulse falls after this second rise it may however remain permanently a few beats above the normal. 3rd. When both bandages are suddenly removed there is an instantaneous and usually remarkable quickening of the heart-beat, which only lasts for a very short time, and which is followed by a fall to below the normal rate, and sometimes by irregular action of the heart; this condition is usually of brief duration.

We shall now give the more important data obtained in four of our experiments.

Exp. 1. July 20, 1876. Subject of experiment, *A*. *A* is 22 years of age, weighs 140 lbs., and is 5 ft. 6 in. in height.

Time. p.m. H. M. S.	Pulse Rate in 60 Seconds.	Observations.
1 15	82	*A* has stripped and is lying on a bed, sufficiently covered not to suffer from cold. Sphygmographic tracing of right radial taking.
1 22	78	
1 24	82	Application of Esmarch bandage to left leg is commenced.
	96	During the bandaging.
1 29	88	The bandaging of the left leg completed.
1 30	84	
1 32	88	Sphygmographic tracing taken.
1 32 30	84	
1 37		Bandaging of right leg commenced.
1 40	100	The right leg is half bandaged.
1 41	84	Bandaging finished.
1 44	94	
1 47	92	
1 49	86	
1 50	82	
1 51		Bandages suddenly removed.
	108	
1 54	94	
1 55	70	
1 58	76	
1 59	74	
2 0	76	
2 4	72	

Exp. 2. July 20, 1876. *B* experimented upon. *B* is 22 years of age. Weight of *B* 168 lbs.; height of *B* 6 ft.

Time. p.m. H. M. S.	Observations.	Pulse Rate in 60 Seconds.
3 45	*B* is lying on a bed stripped.	58—62
3 52	... ...	64—66
3 53	Bandaging of right leg commenced.	56
3 58	Bandaging is proceeding.	72
3 58 30	Bandaging is completed.	72
4 1	Sphygmographic tracing taken.	58
4 6	Bandaging of left leg commenced.	58
4 9	Bandaging is proceeding.	68
4 12	Bandaging finished. Feels fulness of head. Sphygmographic tracing taken.	60
4 15	... ...	62
4 19	Both bandages simultaneously removed. In the two succeeding half-minutes the pulse was 44 in 30 seconds	88
	42 „	82
4 24	... ...	58

Appended is the set of sphygmographic tracings. It will be observed that in this case tracings (2) and (3) do not indicate any quickening of the pulse, the rate of which had fallen before the tracings were taken.

Tracings (4) illustrate well the quickening which immediately follows the return of blood to the limbs. It will be observed that the lowest of the three tracings in (4) shews a much more rapid pulse than the second and third; in the few seconds which elapsed between the taking of (1) and (3) the frequency of the pulse had diminished remarkably.

Tracings (5) illustrate how perfectly the pulse returned to its normal rate and form after the bandages had been taken off.

Tracings taken in Exp. 2. *B.* July 20, 1876.

Fig. 1. Normal, before bandaging.

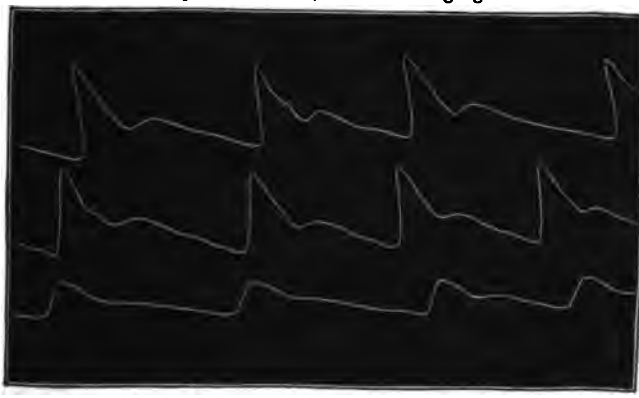


Fig. 2. After one leg has been bandaged.

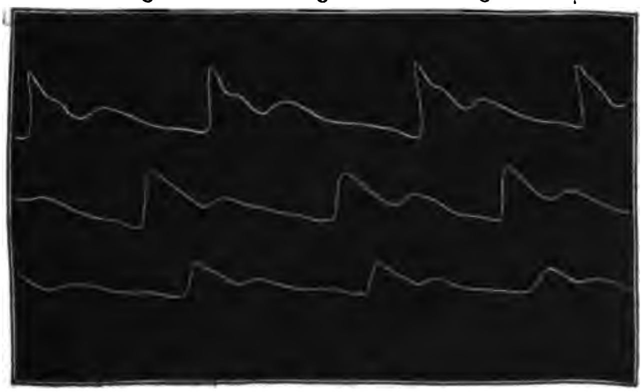


Fig. 3. After both legs have been bandaged.

Fig. 4. Immediately after unbandaging.

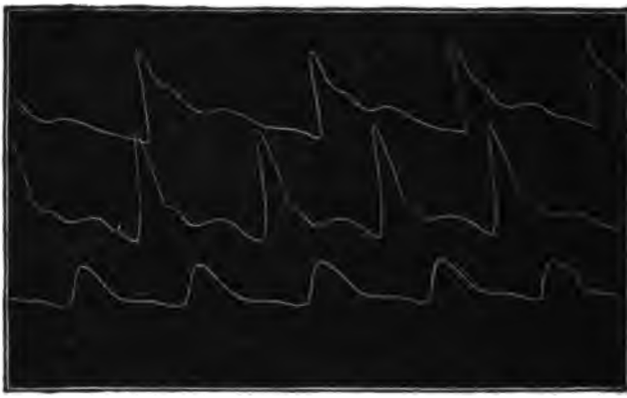


Fig. 5. Some time after unbandaging.

In all cases the lowest of the three tracings which was taken first is at a pressure of 3 oz., the middle curve at 4 oz., and the highest curve at 5 oz.

Exp. 3. May 19, 1876. Individual experimented upon, *C.* Age of *C* is 21; weight 140 lbs.; height 5 ft. 11½ in.

Time. p.m. H. M. S.	Observations.	Pulse Rate in 60 Seconds.
8 5 to 8 12	Is lying recumbent on a bed.	70—74
8 16	... ...	62
8 17 15	... ...	63
8 19	... ...	66
8 23	Bandaging of left leg commenced. Pulse during each successive 30 seconds throughout the bandaging counted 36 in 30 seconds.	
	35 "	
	39 "	
	38 "	
	37 "	
	44 "	
	44 "	
	or at the rate of	88
8 39	Bandaging is completed.	68—70
	Complains of fulness of eyes.	72
8 41	... ...	70
8 50	Anæsthesia of left foot.	
8 51	Bandaging of right leg commenced.	62
8 53	Pulse 35 in 30 seconds.	
8 53 30	35 "	
8 54	38 "	
8 54 30	38 "	76
8 55	36 "	
8 55 30	38 "	
8 59	44 "	
8 59 30	48 "	92
9 0	45 "	
9 1	45 "	90
9 3	Bandaging completed.	
9 4 30	Pulse 36 in 30 seconds.	
9 5	34 "	
9 5 30	34 "	
9 6 45	37 "	
9 7 15	37 "	
9 7 45	Suffering a little from palpitation.	70
9 8	... ...	66
	Left leg unbandaged.	
9 12 30	... ...	72
9 14 30	Right leg unbandaged.	
9 15	Shivering of whole body, but without any feeling of cold.	68
9 16	Shivering and tremor of all the muscles. ...	69
9 17	Chattering of teeth.	

Exp. 4. *C* was experimented upon exactly as before.

	H.	M.	S.	
At	2	55		Bandaging of right leg was commenced.
	2	59		Bandaging of right leg completed.
	3	5		Bandaging of left leg commenced.
	3	10		Bandaging proceeding; complains of fulness of eyes.
	3	12	30	Bandaging of both legs completed.
	3	23		Both legs unbandaged.

As the tracings in this case illustrate more visibly the quickening which immediately followed bandaging of first and second leg, they are given without a table of pulse-rates. Tracing (4) does not shew the quickening which followed unbandaging, too long a time having elapsed between this event and the taking of the tracing. The pulse was however observed to rise from 78 to 92 in the minute following unbandaging.

Tracings taken in Exp. 4. *C.* July 20, 1876.

Fig. 1. Normal, before bandaging.

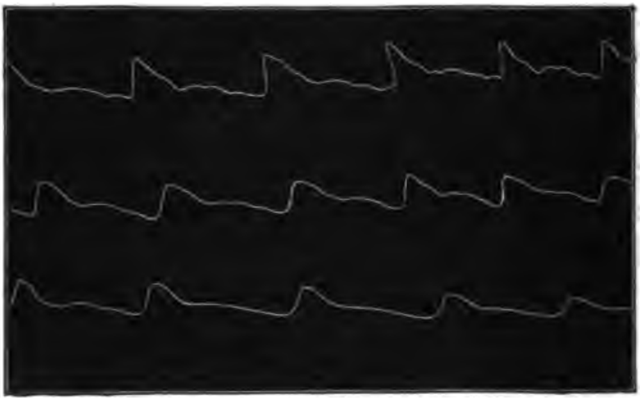


Fig. 2. After one leg had been bandaged.

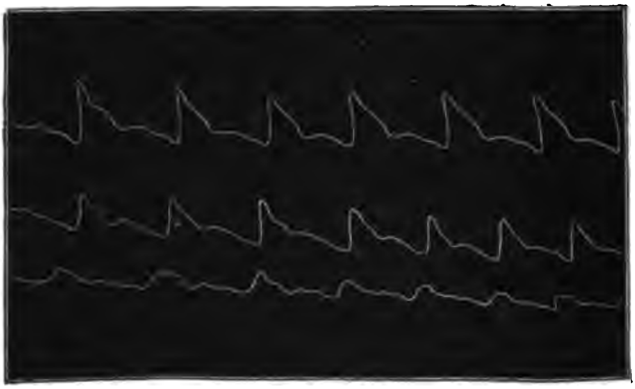


Fig. 3. After both legs had been bandaged.

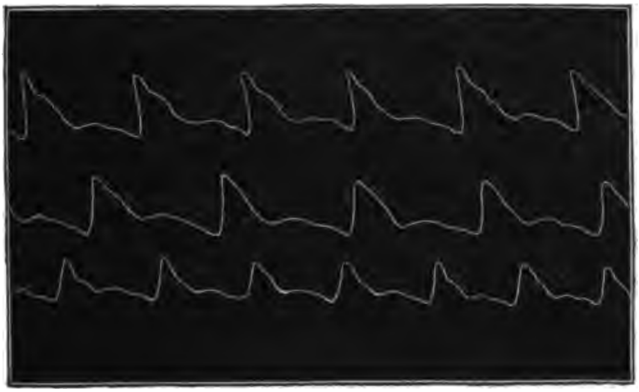
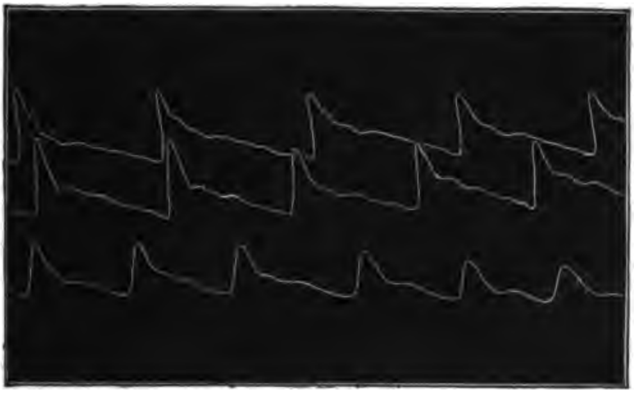


Fig. 4. After unbandaging both legs.



In all cases the lowest curve, which was taken first, is at a pressure of 3 oz., the middle curve at 4 oz., and the highest curve at 5 oz.

Analysis of the changes induced in the Experiments.

Having illustrated by a sufficient number of facts the phenomena which were observed to follow the expulsion of blood from the limbs by Esmarch's method, we think it well to examine the influence which the bandaging and unbandaging must exert upon the blood-pressure in arteries and veins.

When Esmarch's bandages are applied to one or both lower extremities the following results must follow.

Firstly. Blood is expelled from the capillaries and veins of the compressed part. The cadaveric whiteness of the part is a proof of the emptying of the capillaries. It is certain that nearly the whole, if not the whole, of the blood contained in the limbs is expelled by Esmarch's method[1].

Secondly. Blood is expelled from the arteries, part of it passing into capillaries and veins, but part also being pushed back into the arteries of the trunk.

Thirdly. Lymph is expelled from the lower extremities in considerable quantity, and increases the amount of lymph emptied into the venous system.

There can, we believe, be no doubt that the effect of these three sets of events must be to increase for a time the pressure in the venous system to a greater extent than the pressure in the arterial system. Our reasons for this belief are briefly the following:—

The amount of blood contained in the capillaries and veins of the limb, or even in the latter alone, is very much greater than that contained in the arteries, so that if the effect of the bandaging were merely to add arterial and venous blood to the arteries and veins of the trunk, we should say that more venous than arterial blood entered the trunk as the result of the bandaging. But the effect of the quantities of arterial and venous blood thrown into the body upon the pressure in the right and left sides of the heart cannot be measured merely by their relative amounts; we must take into consideration likewise the capacity of the portion of the vascular system which has the extra quantity of blood added to it. Now any increase of pressure at any point of the arterial system may affect more or less, it is true, the blood-pressure in the arteries of all parts; not so with the veins, for the blood which is thrust into say the iliac veins, when one lower limb is compressed, will have no influence on the blood-pressure in the veins of the other lower limb or of the upper extremities. The presence of valves will limit the increase of pressure due to this addition of blood mainly to the veins of the trunk; we should therefore assume

[1] Labord and Mord d'Arlaux state from their own experiments that the veins are not completely emptied by the compression; M. Krishaber asserts that in man there is found to be an entire abser ce of blood in the veins.

that, notwithstanding the greater capacity of the veins as compared with the arteries of the trunk, the effect of the application of Esmarch's bandages to both lower limbs will be *for a time* sensibly to increase the relative pressure on the right side of the heart.

The addition of lymph forced out of the compressed lower limbs will tend to increase still further the relative venous pressure—it will have, however, another effect which must not be neglected; the effect to which we allude is a modification of the chemical characters of the blood of the right side. It is indeed possible that a small increase in the amount of lymph entering the great veins may exert a marked influence upon the action of the heart, as this organ is now known to be exceedingly sensitive to very minute differences in the chemical composition of the blood supplying it[1].

On the other hand, when Esmarch's bandage is removed the effect is suddenly and extensively to increase the vascular area by adding to the vessels of the trunk and upper extremities the vessels of both lower limbs. But again, the change does not equally affect the arterial and venous systems. Owing to the inter-position of valves it may be asserted that the accession of area affects merely the arteries. In consequence, the arterial tension suddenly diminishes while the venous tension is not immediately touched; the *relative* pressure in the right heart as compared with the left, has increased; in other words the normal *difference* of pressure between the two sides of the heart is lessened; and, in fact, the same change, but otherwise induced, has occurred after unbandaging as after bandaging.

Theoretical explanation of the Phenomena.

It is with diffidence that we trust ourselves to speculate at all in this matter: not only on account of the presence of an unknown factor in the effect on the heart of the added lymph: but also on account of our imperfect, merely general, knowledge of the action of afferent nerves in reflex connection

[1] This influence of the lymph as affecting the *quality* of the blood and thus influencing the action of the heart was pointed out to us by Professor Kronecker when an abstract of this paper was read before the Physiological section of the British Association in September, 1876.

with the heart. Is it not possible, for example, that the changes we have observed may be due to the stimulation of afferent nerves, other than sensory, ramifying in the tissues of the leg—a stimulation determined by the expulsion and readmission of blood? But setting aside the possibility that further discovery may suggest additional causes of the phenomena, the hypothesis we are about to advance appears competent to connect the facts already observed, and may turn out to be at least a partial explanation.

It has been stated that bandaging and unbandaging the lower limbs produce the same series of effects on the pulse-rate. It has further been shewn that both operations lead to disturbances of vascular tension exactly similar in nature though differently conditioned: that is to say, in both cases, the difference which normally exists between the venous and arterial pressures is diminished, on bandaging, by approximating the venous to the arterial, and on unbandaging, by approximating the arterial to the venous pressure.

May we not seek in this coincidence of conditions the cause of the altered heart-rate? In order to do so it must be assumed that such a diminution of the normal difference of venous and arterial pressures leads to accelerated pulsation of heart. This assumption is not so important as it may at first sight appear: for it is but a more general expression of a proposition advanced long ago, and often insisted upon by Professor Marey.

M. Marey has shewn that when the arterial pressure is increased the heart beats more slowly; when the arterial pressure is diminished the heart beats more rapidly. He has cited a large number of cases, which shew that all those acts of the body which lead to vascular dilatation are necessarily accompanied by a rapid action of the heart. Thus when we run the muscular vessels dilate and the heart beats rapidly. When the body is heated the same effect follows, whilst when it is cooled the heart beats more slowly. Now we may, if we like, say that in these cases the primary cause of the rapid or slow heart-beat is the diminution or increase of the arterial pressure; we believe, however, that it is not unlikely that the proximate cause is to be found in the increase or diminution of the pressure in the right side of the heart.

In all the cases quoted by M. Marey in which the heart beats more rapidly, the normal difference in pressure is diminished: *i.e.* the pressure in the right side is relatively increased, and in all the cases in which the heart beats more slowly the pressure in the right side is relatively diminished. Thus dilated arterioles permit the blood to flow rapidly and in larger quantity into the veins, thus lowering the arterial and raising the venous tensions, and so reducing the difference normally existing between them. On the other hand, contracted arterioles have just the opposite effect.

This hypothesis, therefore, at the outset, receives much support from the facts and arguments of Professor Marey. But it does not lean solely upon them. In the first place, the experiments of Blasius on the work done by the frog-heart prove that, in the frog-heart, when the arterial pressure is constant the heart-rate, up to a certain point, increases as the venous pressure.

In the second place, in the pathological conditions which lead to an engorged right side, the heart's action is permanently quickened: for example, in mitral stenosis, whenever there is venous engorgement, the heart beats more rapidly.

Thus, if the view proposed of M. Marey's law be accepted, the experiments of Blasius and the case of mitral stenosis, not before covered by the law, are brought into relation with the well-known effects of increased or diminished arterial tonus, as well as with our own observations.

The various facts of the present research are accounted for in the following manner:

1. When the limbs are compressed, the quickening is explained by a diminution of the normal difference in the blood-pressure *due to the increase of pressure on the right side.*

2. The return to the normal or to near the normal rate after one limb has been compressed is due to the fact that the normal relative difference has been re-established.

3. The quickening when the limbs are unbandaged is due to a diminution of the normal difference in the blood-pressure, *owing to a decrease of pressure in the left side.*

It is quite conceivable that in the first case the right side of the heart may initiate the more rapid contractions of the whole organ, and that in the second case the left side may do so[1].

[1] The reader is referred to a paper which has appeared since this article was written, entitled, "Ueber die Abhängigkeit des Herzrhythmus von den Blutdruckschwankungen von Dr S. Tschiriew in St Petersburg:"—*Centralblatt für die medicinischen Wissenschaften*, 1876, No. 35, p. 609. The author has observed an acceleration of the heart to follow, when compression of the abdominal aorta has been kept up, and is then stopped.

ON THE EFFECTS OF SULPHATE OF ATROPIA ON THE NERVOUS SYSTEM OF FROGS. By SYDNEY RINGER, M.D., *Professor of Therapeutics at University College*, and WILLIAM MURRELL, L.R.C.P., *Sharpey Physiological Scholar.*

IN the course of an experimental investigation made with the view of elucidating the true nature of tetanus, we had occasion to repeat many of Dr T. R. Fraser's well-known experiments on the influence of atropia on the nervous system of frogs. We are induced to publish our observations; for though in the main they are confirmatory of those of previous observers, they differ from them in some respects.

In the first place we will speak of the tetanizing action of atropia. Dr Fraser has shown (1) that in frogs tetanic symptoms follow the subcutaneous injection of a dose of sulphate of atropia equivalent to about 1000th of the weight of the animal; (2) that this tetanus sometimes sets in on the second day, but more frequently on the third, fourth, or fifth; (3) that it varies in its duration from a few hours to seventeen days; (4) that it is due to the action of the drug on the cord (*medulla oblongata* and *medulla spinalis*).

The observations were made during the months of May, June and July. The frogs used for our experiments were with a few exceptions the ordinary *Rana temporaria*. We employed, except when the contrary is stated, a 1 in 20 solution of sulphate of atropia in water, the requisite dose being injected either under the skin of the back or into the axilla. The first twelve cases were observed thrice daily, between seven and eight in the morning, one and two in the afternoon, and five and six in the evening. In the subsequent experiments, observations were made much more frequently, with the view of determining how rapidly paralysis occurred, how soon it reached its height, and how quickly it declined. In some cases the animal was under almost continuous observation for many hours, in others the notes were taken every eight or ten minutes for the first hour, and hourly or every three hours subsequently. We may take this opportunity of explaining that whenever we employ the term

"pithed and pegged" we mean division of the cord by cutting, and destruction of the brain by the introduction of a piece of wood into the cranial cavity. We, like Dr Fraser, often obtained strong tetanus from the subcutaneous injection of atropia, but found that his dose (from $\frac{1}{735}$ to $\frac{1}{1250}$ of the weight of the frog) usually killed our animals instead of producing the desired result. With a smaller dose, however, namely, from $\frac{1}{1500}$ to $\frac{1}{2000}$, we were more successful. The tetanus in our experiments commenced earlier than in Dr Fraser's, our average period of onset being 20 hours; in one case it was well marked in 3 hours, whilst in the longest delayed it was 28 hours. With us, too, it lasted for a shorter time, for in one animal it continued only eight hours, and never in any instance exceeded five days. We imagine that these differences are due to the time of the year at which the observations were made. In the following table we give a summary of these experiments:—

TABLE I.

Why is the tetanus so long delayed after atropia poisoning? One writer, referring to Dr Fraser's paper, says that the paralysis of the motor nerves prevents the tetanic condition of the cord from displaying itself on the muscles, but Dr Fraser himself nowhere makes this assertion, and indeed his cases prove the contrary.

This proffered explanation we hold to be erroneous for the following reasons:—

I. Bezold and Bloebaum have shown that even with very large doses it is difficult to destroy completely the conducting power of the motor nerves, and it is obvious that as long as their conductivity is in the smallest degree retained, the tetanic condition of the cord must produce more or less tetanus of the muscles.

II. The onset of tetanus is delayed even in cases in which the dose of atropia is so small as to produce but slight paralysis, and it must be admitted that if the motor nerves are capable of conveying voluntary and normal reflex impressions they can conduct tetanic reflex stimuli. Thus in many of Fraser's cases there was never complete loss of reflex and voluntary power during the period which elapsed between the injection of the drug and the onset of tetanus. It will be found that of the cases in which he obtained tetanus there were twelve in which

										were decidedly less in the ligatured leg, and continued so. Tetanus always stronger in the left (unprotected) limb. Begun at the same time in both limbs. Irritation of any part of the body excites it.
42	31	$\frac{1}{4}$	$\frac{1}{1918}$	Slight	5 hours	23 hours	5 min.	10 min.	Incomplete	Right femoral artery and vein tied. Reflex action and voluntary power weaker in the protected than unprotected limb. Tetanus begun at the same time in both hind limbs, and was equal in both.
43	19	$\frac{1}{8}$	$\frac{1}{1466}$	None			2 min.	10 min.	Complete	Right femoral artery and vein tied. Reflex action and voluntary movement, before and after poisoning, weaker in the right leg.
							5 min.	5 min.		

the paralysis was incomplete; that in seven of the thirteen in which it had been complete, a partial recovery of reflex and voluntary power had taken place for a day or more before the onset of the tetanus. In eleven of our own twenty-six cases there was incomplete paralysis of reflex action and voluntary power, and in all these cases the onset of tetanus was delayed. In two cases, indeed, both voluntary and reflex power had been completely regained before the tetanus set in. In one case in which there had been complete paralysis, it began to improve five and a half hours before the commencement of tetanus.

III. If the poison be prevented from having access to certain limited regions by ligature of the nutrient vessels, the onset of tetanus is still delayed even in these protected parts. Fraser gives an account of four experiments, in which he adopted this mode of procedure. In three he tied the femoral vessels, and in one the abdominal aorta, before poisoning the animal, and yet tetanus did not occur in the protected limbs till twenty-two hours, fifty-one hours, three days, and twenty-two hours respectively.

We have tested the action of atropia on ten pithed and pegged frogs, in which, before poisoning, the abdominal aorta had been tied. The following was our mode of procedure:—We first divided the medulla by cutting through the occipito-atlantal membrane, and then passed a pointed wooden peg upwards through the foramen magnum into the skull, so as to destroy the brain. We then placed the animal on its back on the frog-board, and cut through the abdominal wall on one side, usually the left, taking care to avoid the abdominal vein. The intestines were then drawn aside, and the abdominal aorta having been slightly raised, was ligatured just above its bifurcation. The walls of the abdomen were brought together by sutures, and when the animal had recovered from the shock of the operation we injected our sulphate of atropia solution under the skin of the back. At the conclusion of our experiment we always ascertained by a careful post-mortem examination that the vessels had been securely ligatured. In every instance in which more than two or three drops of blood were lost, the operation was deemed unsatisfactory, and the animal rejected.

We give the results of these experiments in the following table:—

TABLE II.—*Observations on Pithed and Pegged Frogs with ligature of the abdominal aorta.*

Number of frog.	Weight in grammes.	Dose of sulphate of atropia in grains.	Proportion between dose and weight of animal.	Degree of tetanus.	Tetanus set in.	Tetanus lasted.	Loss of reflex action begun.	Loss of reflex action at its height.	Degree of loss of reflex action.	
27	32	$\frac{3}{20}$	$\frac{1}{3292}$	Strong	25 hours	52 hours	12 min.	27 min.	Nearly gone	Heart continued beating 3 days.
28	21	$\frac{3}{20}$	$\frac{1}{2160}$	Marked	9 hours	72 hours	12 min.	37 min.	"	" " " "
29	18	$\frac{3}{20}$	$\frac{1}{1851}$	None			20 min.		"	" " " "
30	20	$\frac{3}{20}$	$\frac{1}{2057}$	None			40 min.		"	" " " 2 "
31	18	$\frac{3}{20}$	$\frac{1}{1851}$	None			5 min.	48 min.	Quite lost	
32	20	$\frac{3}{20}$	$\frac{1}{2057}$	None			10 min.	42 min.	"	
33	16	$\frac{3}{20}$	$\frac{1}{1646}$	None			5 min.		"	
34	16	$\frac{3}{20}$	$\frac{1}{1646}$	None			5 min.		"	
35	19	$\frac{3}{20}$	$\frac{1}{1954}$	Marked	$4\frac{1}{2}$ hours	24 hours	5 min.			Tetanus occurred as early and as marked in anterior as posterior parts of the body.
36	25	$\frac{3}{20}$	$\frac{1}{2572}$	None			7 min.			
						Average	12 minutes	38 minutes		

It will be seen from the table that in the three cases in which we obtained tetanus it was delayed for 25 hours, 9 hours, and 4½ hours respectively.

In seven cases we tied the femoral vessels in the upper third of the thigh. Our mode of procedure was as follows:—We pithed and pegged the animal in the usual way, and having placed it in a prone position, carried an incision through the skin on the outer side of the thigh, when the vein coming into view was readily secured. By gently separating the muscles the artery was then seen and was tied as near the abdomen as possible, care being taken not to touch or otherwise injure the nerve. Finally the skin was brought together by a few sutures, and the operation was complete. In these cases the fact of the vessel having been securely ligatured was confirmed not only by the post-mortem examination, but usually by comparing by the aid of the microscope the condition of the circulation in the webs of the two feet. The details of these experiments are given in Table III.

It will be seen from the foregoing table that in the three cases in which we obtained tetanus, it occurred simultaneously in the two legs. In two cases it was equal in degree in the two legs, and in the third case it was stronger in the poisoned than in the unpoisoned limb.

We conclude then for these reasons that the late occurrence of tetanus in atropia poisoning is not due to paralysis of the motor nerves, but that it is owing to the cord being slowly affected. It appears that whilst the poison very quickly paralyses, it takes many hours, or even days, before it tetanizes.

In our experiments we obtained some rather unexpected results. Thus our observations lead us to conclude that atropia paralyses much more through its depressing action on the spinal cord than on the motor nerves. It is well known that considerable difference of opinion prevails on this point, some experimenters attributing the paralysis chiefly to the action of the poison on the motor nerves, and others to its action on the cord. Fraser in his article "On the connection between Chemical Constitution and Physiological Action," Part II, says, atropia "produces paralysis chiefly by affecting

the motor centres and sensory nerves," and our observations confirm this conclusion in respect of the motor centres (spinal cord).

Thus in the experiments we have recorded in this paper, after tying the abdominal aorta, or the femoral artery and vein, and then poisoning the animal, we found that paralysis set in as early, progressed as quickly, and became as complete in the ligatured as in the unligatured, and consequently poisoned limb.

It occurred to us that perhaps our experiments were made at a different time of year to those performed by other observers, and that this might account for the difference in our results. Our first observations were made in May, June and July, but with the view of solving the point we repeated many of them during the month of November. We tied the femoral artery and vein of the right leg of two frogs, and then poisoned them by injecting sulphate of atropia under the skin of the left axilla. To one we gave a dose too small to produce complete paralysis; to the other a much larger dose, namely half a grain, which caused complete paralysis in two minutes. In the frog to which the small dose had been administered, both posterior limbs were almost completely paralysed, but the ligatured limb was a little the stronger after the poisoning. In the frog with the large dose, both hind limbs were absolutely paralysed in two minutes. We feel bound, therefore, to conclude that sulphate of atropia paralyses in great part by its action on the spinal cord.

Does atropia exert its action directly on the cord, or only indirectly through its influence on the heart and circulation? Is it a spinal depressant, or are the phenomena we have witnessed simply due to its action as a cardiac poison?

Atropia powerfully depresses the heart, slowing or even completely arresting its action. Even in cases in which the number of pulsations is reduced by only a half the heart does very little work, for on examination it is found that during diastole it becomes but slightly distended with blood, so that the circulation must be in reality almost at a standstill. That such is the case is also shown by a microscopic examination of the web of the foot, when the blood will be seen to be either

stationary, or to be moving very slowly in a few only of the larger vessels. It occurred to us, this effect on the heart and circulation might cause the paralysis of the spinal cord.

Vulpian found that ligature of the aorta just above the heart suspended, in the course of a few hours, the excitability of the cord, and soon after impaired the conductivity of the motor nerves. The paralysis from atropia poisoning, however, comes on very much more quickly than this, a circumstance which at first sight appeared at once to solve the question, and to show that atropia exerts a specific, or primary action on the cord. It occurred to us, however, that it was not improbable that in summer when nutrient changes in frogs are performed much more rapidly than in winter, the functional activity of the cord might be sooner affected by arrest of the circulation. We determined, therefore, to repeat Vulpian's experiment in a modified form. We tested the condition of reflex action and voluntary movement in eight frogs, in which the circulation had been arrested by mechanical means. In two of these cases the heart was cut or torn out from the chest, and in the remaining six the aortæ were securely ligatured just above their origin from the bulb. The latter operation was performed as follows:—The animal was pithed by cutting across the medulla, and pushing a spigot of wood through the foramen magnum into the cranial cavity. When the effects of the shock had completely passed off, we pinned the (brainless) animal down on its back, and opened the thorax, by elevating the lower end of the sternum and cutting through the adjacent soft tissues. The heart was then seen beating, and the pericardium having been opened, no difficulty was experienced in slipping a ligature under the aortæ close to the bulb, and tying them simultaneously. Finally, the sternum was replaced, and the edges of the incision were brought together with a few sutures. The operation was usually performed in a very few minutes, and in most cases not a single drop of blood was lost. The experiment of arresting the circulation by removing the heart was even simpler. The brain having been destroyed as before, the thorax was opened by one cut of the scissors and the heart was seized in the forceps, and at once removed. We may mention that the success of the operation was confirmed

by a post-mortem examination, although such a step may hardly appear to have been necessary.

As the result of these experiments, we found that, on an average, the impairment of reflex action commenced in 13 minutes, and that the paralysis was complete in 37 minutes. It will be seen that our results differ considerably from those of Vulpian, a discrepancy which we then thought might possibly have been due to the season, and the condition of functional activity of the frogs, although our subsequent experiments have shown that such is not the case. As our experiments on circulation were made at the same time, and under identically the same conditions as our observations on atropia, they are obviously the best fitted for purposes of comparison.

By reference to the table (Table II.) giving the results of poisoning by atropia in frogs in which the lower limbs had been protected by ligature of the abdominal aorta, it will be seen that in four of these cases loss of reflex action was complete on an average in 38 minutes. These results accord in the most striking manner with those already described as resulting from the mechanical arrest of circulation, and they might be considered to afford a strong proof that the cardiac action of atropia is sufficient to account for the paralysis of the cord produced by this drug. Such, however, is not the case, for on examining the table it will be found that our experiments are in some respects unsatisfactory. The dose of atropia administered was small, so small, in fact, that in two cases the paralysis was never complete. It was therefore obviously necessary to ascertain whether larger doses would not produce complete paralysis in a shorter time. The experiments necessary for the elucidation of this point were made in November, and the opportunity was taken of instituting a series of comparative observations with the view of determining the effects of mechanical arrest of circulation in producing complete paralysis in brainless frogs. These results are given in the accompanying table:—

TABLE III.—*Pithed and Pegged Frogs poisoned with Atropia.*

Date.	Weight of frog.	Amount in grains of sulphate of atropia.	Proportionate dose.	Paralysis complete.
Nov. 29	20 grammes	$\frac{1}{6}$	$\frac{1}{617}$	2 minutes
"	24 "	$\frac{1}{5}$	$\frac{1}{617}$	4 minutes
"	30 "	$\frac{1}{10}$	$\frac{1}{1548}$	9 minutes
"	20 "	$\frac{1}{6}$	$\frac{1}{1548}$	3 minutes
			Average	4·5 minutes

Table showing the effect of mechanical arrest of circulation in pithed and pegged frogs.

Nov. 29				24 minutes
"				55 minutes
"				24 minutes
			Average	34 minutes

In these observations, sulphate of atropia caused, on an average, complete paralysis in 4·5 minutes, whilst mechanical arrest of the circulation required, on an average, 34 minutes. In the first of the atropia cases recorded in this table, we tied the femoral vessels before poisoning, and yet the paralysis became complete in both posterior limbs in 2 minutes.

We conclude, then, that atropia has a direct paralysing action on the cord, and does not affect it through its depressing action on the circulation.

In a paper in the volume of the *Medico-Chirurgical Transactions* for 1876, we have endeavoured to show that tetanus is not due to stimulation or an excited condition of the cord, but to a diminution or loss of resistive force in the reflex portion of the cord. This resistive force localizes the impressions conveyed through the nerves to the central nervous system, and when it is destroyed an impression can diffuse itself throughout the cord and produce a general evolution of force, which being conveyed by all the motor nerves to every muscle, produces tetanus.

We believe that the action of atropia confirms this view, or

at least is strongly opposed to the current notion that tetanus is due to an excited condition of the cord. Thus atropia, we believe, depresses the cord very powerfully. The resulting paralysis, which after moderate doses passes off in the course of a few hours, is followed by tetanus, sometimes in twenty-four hours, and at others much later. Now it appears to us almost inconceivable that a remedy should first paralyse the cord and then many hours later stimulate it. It may be urged that this delay in the appearance of the tetanus depends on the primary depression of the cord, and that the tetanus cannot occur till the paralysis has disappeared. This objection is obviously insufficient, for after a small dose of atropia the partial paralysis ceases in a few hours, or even in an hour, and the animal then seems quite well, but nevertheless the tetanus is delayed for twenty-four or more hours. Again, if this explanation is true, then the tetanus should never occur till the paralysis has disappeared, but this, though generally true, is not always the case, especially in frogs pithed and pegged before poisoning; for in these animals it often happens that paralysis, though far from complete, continues, and after some hours tetanus supervenes, at first very slight, so that a strong irritation excites tetanus, but a weaker irritation a coordinated reflex act. If tetanus depends on a stimulated condition of the cord, coordinated reflex acts should improve on the onset and with the increase in the amount of tetanus, but in reality the very reverse happens, for as tetanus grows stronger, coordinated reflex action simultaneously grows weaker and weaker.

Again, when unmutilated frogs made tetanic with atropia die, the tetanus continues to the last, growing weaker and weaker. This is still better seen in pithed and pegged frogs, for in them the tetanus also continues till all reflex action ceases. Now if tetanus depends on a stimulated condition of the spinal cord, it is obvious that as the cord gradually dies and consequently its functions become depressed, tetanus should cease, and give way to normal coordinated reflex action, but this does not happen; for on the contrary the tetanus grows weaker and weaker, still however, persisting until all reflex action becomes extinct. We have thus in atropia a drug that in large doses produces in pithed and pegged frogs progressive loss of power in the

cord, then after 24 or more hours tetanus sets in, which gradually increases in severity, coordinated reflex action simultaneously declining. We have, indeed, according to prevailing views a drug which paralyses the cord, and then after many hours the paralysis continuing or progressing it stimulates the cord.

When the paralysis is only slight, or when the animal completely recovers from it, then tetanic contractions of the muscles far exceed the amount of muscular action occurring in a natural coordinated reflex act; that is to say, during the tetanic paroxysm, there occurs a far greater discharge of nervous force in the cord than occurs in a normal coordinated reflex act, and this fact might be thought sufficient to justify the term stimulation of the cord. We have, however, already shown elsewhere that this view is probably incorrect.

When the paralysis is considerable and continues till the tetanus supervenes, the tetanic contractions are slight and the discharge of nervous force in the cord is probably less than occurs in a natural coordinated reflex act, and we have then paralysis with weak tetanus. The explanation of this combination is that atropia paralyses the reflex function as well as the resistive power of the cord. The paralysis of the reflex function of course weakens reflex action, whilst the paralysis of the resistive power allows a stimulus to spread throughout the reflex region of the cord, and hence every muscle becomes contracted and tetanus is produced; but as the reflex function is depressed the tetanus is weak.

In atropia we have a drug which quickly paralyses the reflex function of the cord, but requires a much longer time to diminish the resistive power of the cord; hence paralysis precedes and may even disappear some hours before the onset of tetanus.

A CONTRIBUTION TO THE HISTORY OF DEVELOPMENT OF THE GUINEA-PIG. By E. A. Schäfer, *Assistant-Professor of Physiology in University College, London.* (Plates x. and xi.)

(Continued from Vol. x. p. 777.)

Condition of the blastodermic layers, as shown by transverse sections.

a. Region of the allantoid projection.—At the posterior part of the embryo, in the region of the allantoid projection, two only of the blastodermic layers are seen—the hypoblast and mesoblast. The mesoblast forms a strongly marked thickening, composed entirely of the loosely arranged cells, characteristic of the middle layer, with numerous hollowed-out spaces and canals amongst the cells. These spaces and canals are no doubt developing blood-vessels, but at present they have no blood-corpuscles in their interior, differing thus from the blood-vessels which are forming in the parietal mesoblast (see former part), and agreeing with certain vessels, afterwards to be noticed, which are developing in the mesoblast of the anterior region of the embryo. The hypoblast is formed of a single layer of the large, columnar, vacuolated cells previously described and figured: it passes smoothly over the mesoblast without extending at all into the allantoid projection.

b. At the hinder end of the epiblastic or amniotic vesicle. Region of the primitive groove.—As was clearly stated by Bischoff, and has been pointed out in the previous part of this paper, the epiblast forms a distinct closed vesicle at that pole of the ovum which is farthest from the attachment to the uterus (Plate xi. fig. 5, *e. v.*). The vesicle is of an elongated lenticular shape, its roof or embryonic part[1] being composed of characteristic epiblastic cells, two or three deep near the mesial line but thinning off towards the sides; its floor of but a single stratum of flattened cells, fusiform in section, and in contact below with

[1] The guinea-pig embryo being, so to speak, developed upside down, the language of the description is modified accordingly.

a similar layer of mesoblastic cells; the two together forming, as seen already in the longitudinal sections (Vol. x. Plate xxx. fig. 3), the amnion, *am*. At the hinder end of this vesicle the epiblast therefore first makes its appearance in the transverse sections, forming a closed ring (Plate x. fig. 1). The lower part of the ring is a simple layer of flattened cells—the amniotic epiblast; from the margin of this the epiblast gradually becomes thicker as it is traced inwards, and at the centre of the upper part of the ring, corresponding with the axis of the embryo, there is a distinct indentation, the section of the primitive groove, *p.g.* At the groove, the epiblast, much thickened and composed of closely packed small rounded cells, extends towards the hypoblast, and on either side is continued into the mesoblast. According to the ordinary mode of viewing the relations of the blastodermic layers in this region it might be stated that the epiblast and mesoblast become fused together opposite the primitive groove, but, as will immediately be pointed out, the tissue which extends from the primitive groove to the hypoblast must, strictly speaking, be looked upon as purely epiblastic, and it is only on either side, and probably also posteriorly, that there is a continuation of this epiblast into the mesoblast. The appearances observed can best be explained on the supposition of the formation of the mesoblast by an outgrowth from the axial thickening of the epiblast. This supposition, which nearly coincides with the view recently enunciated by Kölliker as to the development of the middle layer of the blastoderm, is strengthened by observations which I have myself made, and which will afterwards be referred to. The hypoblast, in sections from this region, forms as before, a simple layer, easily becoming detached, and composed throughout of a single stratum of flattened cells.

c. Region immediately in front of the primitive groove.—A little in advance of the part from which the section just described is taken the primitive groove disappears, and is succeeded by a region in which there is a slight thickening in the middle line, the thickening being bounded by a shallow groove on either side, and terminating anteriorly by a pointed extremity, the lateral grooves at the same time converging and uniting to form the medullary or neural groove. The axial thickening is

what remains of the anterior end of the primitive streak, and it is here that in the successive sections a very remarkable change can be traced in the relations of the blastodermic layers.

In the posterior part of the region in question the layers have the same relation the one to the other as in the region of the primitive groove (Plate X. figs. 2 and 3). The hypoblast passes over the others as a distinct, easily separable membrane, composed of flattened cells; the axial epiblast presents a considerable thickening, which reaches the hypoblast without blending with it, and is continued without any distinct line of demarcation into the mesoblastic tissue on either side. But the axial tissue is now *obviously* epiblastic in appearance, in spite of its connexion with the epiblast being rather more limited than in the previous sections. And a very little way further in advance (fig. 4) a line of demarcation begins to be traceable between it and the mesoblast on either side—on the one side apparently a trifle sooner than on the other, so that in the succeeding sections (fig. 5, Pl. X.; fig. 1, Pl. XI.) there is no longer any connexion between the two layers, the mesoblast being sharply marked off on either side from the axial thickening of the epiblast. It is seen, however, that the same axial thickening with which in the posterior sections the mesoblast was continuous on either side, and from which it is probable, as before mentioned, that the mesoblast was formed by lateral outgrowth and expansion, now not only comes into close connexion with, but is actually fused with the hypoblast (fig. 1, Pl. XI.), which at this place no longer easily falls away from the other layer as before, but is not even separable by mechanical traction. The axis of the embryo, therefore, is here occupied by a continuous column of cells (*f*), which inseparably connect the epiblast and hypoblast, and, traced from behind forwards, would appear to be chiefly of epiblastic origin. They are small, round, and closely packed, and become stained strongly with hæmatoxylin. They have obviously no longer any connexion with the well-characterized mesoblastic tissue on either side.

Examined yet a little more anteriorly (Pl. X. figs. 6 and 7), the fused axial column is somewhat broader, and at either side, immediately opposite or above the rootlets of the neural groove, a faint line of demarcation is beginning to be traceable be-

tween epi- and hypo-blast (fig. 7). But quite in the middle line the fusion is still complete, and there is here seen in the sections a nest of small cells (fig. 2, Plate XI.) not readily assignable to either epi- or hypo-blast, but bounded laterally by the differentiated parts of both. This central group of cells I was at first inclined to regard as forming the rudiment of the notochord (see previous part, p. 777), and indeed this may after all prove a correct supposition. But considering that most previous observers describe the development of the notochord as commencing at the anterior end of the embryo and proceeding backwards, whereas according to the other view it would be necessary to assume for the chorda a growth forwards underneath the neural groove from the end of the primitive streak; considering also that nearly all the more recent observations[1] point to the conclusion that the notochord arises from a thickening of the hypoblast simply without participation of epiblast (or of mesoblast), it would seem on the whole a more rational view to regard the group in question as a portion of the fused axial column, the cells of which by a continuation from each side of the line of demarcation above mentioned will eventually belong to one or other of the two layers (epi- or hypo-blast).

Assuming then that the axial fusion of epiblast and hypoblast in this region of the embryo has some other meaning than the formation of the notochord, the purpose which it may subserve is by no means clear. Traced backwards the fused axial tract is no doubt continuous in great part with the epiblastic thickening from which the mesoblast appears to grow, and it might be supposed that in this way hypoblastic elements might concur with the epiblastic in the formation of the mesoblast. But it must at the same time be borne in mind that at the

[1] Balfour, 'Development of Elasmobranch Fishes,' in *Quarterly Journal of Microscopical Science*, Oct. 1874, and in this Journal for July, 1876, p. 683; and Hensen, *Entwickelung des Kaninchens und Meerschweinchens*, in *Zeitschr. f. Anatomie u. Entwickelungsgeschichte*, Bd. I. Kölliker (*Entwickelungsgeschichte*: 2te Auflage) adopts, it is true, a different view of the development of the notochord from that of Balfour and Hensen, ascribing to it a mesoblastic origin; but regarding merely the delineations he gives of his own preparations, it is difficult to understand how the inferences drawn from them could have differed so materially from the statements of the other observers. Dr A. Schulz in a paper received since the above description was written (*Arch. f. Micr. Anat.* Bd. XIII. Heft 1) describes a complete fusion of epiblast and hypoblast in Elasmobranchs and connects the fusion with the origin of the notochord.

part where the fusion of epiblast and hypoblast is complete, there remains no connexion whatever between the axial column and the mesoblast.

d. Region of the neural groove or proper embryonic region.—Immediately in front of the part just considered, the neural groove (Pl. x. fig. 8; Pl. xi. fig. 3, *n. g.*) begins to make its appearance in the middle line as a wide shallow depression formed by the blending of the two grooves which were seen one on either side of the axial prominence of the preceding region. Here the differentiation of the epiblast and hypoblast is complete, and there is a distinct straight line of demarcation between the two layers, which are nevertheless in close contact, and continue so along the whole extent of the neural groove. The mesoblast on the other hand remains as before completely marked off on either side of the region of contact of epi- and hypo-blast; *there is no mesoblast whatever in the axis of the embryo.*

Following the sections forwards more and more (Pl. x. figs. 9, 10, 11) we find the neural groove becoming gradually deeper and narrower, and the epiblast which bounds it considerably increased in thickness. Where it passes over the lateral sheets of mesoblast the epiblast is about two or three cells deep, and maintains its characteristic appearance, but quite at the side it becomes thinner and is diminished eventually to a single layer of cells, which, becoming shorter and more flattened, pass round to form the inner layer of the amnion (as seen also in longitudinal section).

In the sections of the anterior part of the embryonic region (fig. 11, Pl. x.) the epiblast on either side is seen to be separated at one place by (coagulated) fluid from the mesoblast[1]. This appearance corresponds with that previously seen in the surface view of the embryo and which was there termed the *head-fold* (Vol. x. Pl. xxx. fig. 2, *h.f.*), but which it would be more correct to term the *anterior limiting fold* of the blastoderm. It is composed wholly of epiblast without any mesoblastic tissue.

The axial hypoblast (Pl. xi. figs. 3, 4, *a. h.*) consists of a

[1] This fluid is in reality collected, not between the epi- and meso-blast, but between the epiblast and a homogeneous membrane, which in other parts is in close contact with the epiblast and limits it towards the mesoblast.

single layer of columnar cells not very unlike the epiblastic cells (*a.e.*) with which they are in contact (or nearly so). At the posterior part of the embryonic region the layer is thickest, and it gradually becomes thinner as the sections are followed forwards, but the cells keep their columnar character along almost the whole extent of the neural groove. They are bounded above and below by even lines; but at the sides the hypoblast curves upwards to enclose the mesoblast, forming an angle with the axial part, and the columnar cells become gradually shortened into the ordinary flattened hypoblastic cells. This angle is partly occupied by a group (as seen in section) of two or three small flattened cells which extend a short distance over the axial part of the hypoblast (Plate XI. fig. 4, *a'. h'*). The arrangement of the hypoblast is on the whole very similar to that described by Balfour[1] in Elasmobranch fishes as the first stage which the hypoblast passes through when about to give origin to the notochord, and it is possible that the thickening of the axial hypoblast in the guinea-pig embryo may have a similar object. But Balfour describes the thickening in Elasmobranchs as being most marked anteriorly, whereas in this case the hypoblast is thicker at the posterior part. With the exception of this axial thickening of the hypoblast, which may or may not be concerned with the formation of a notochord, there is no trace of such a structure to be seen. The hypoblast passes round at the sides, in the manner already described, to form the external investment of the ovum.

The mesoblast along the whole extent of the neural region is completely differentiated from the other two layers, and quite characteristic in appearance. The lateral sheets are separated throughout from one another by the junction of epiblast and hypoblast at the neural groove. The mesoblast forms an unbroken layer on each side as far as the attachment of the amnion, where it splits into two, as before described, one following the epiblast over the amnion, the other lining the parietal hypoblast. The cells of the mesoblast are much more loosely and irregularly arranged than those of the other two layers, and they appear many of them to possess fine branches. Two variations from the general uniformity of appearance of

[1] *Loc. cit.*

this layer may be noticed. One of these consists in a much looser condition of the tissue, with small clear round spaces, like those seen in the sections of the allantois. This appearance is to be seen in sections from near the middle of the embryo at a part of the mesoblast a short distance from the axis and quite close to the hypoblast. It is perhaps a place where blood-vessels are becoming developed.

The other appearance is observed near the anterior end of the embryo, quite at the sides, and in a part where the mesoblast is only about two layers of cells thick. A split begins to appear here between the mesoblastic cells. Traced forwards in the sections the split (which is bridged across by fine threads) widens out to a fusiform cleft (Pl. X. fig. 11, *sp*), and still further forwards it becomes (sooner on one side than on the other) a well-defined comparatively large, clear, circular aperture (*sp'*), bounded by a layer of cubical cells. It is impossible to speak with certainty as to the nature of the canals which are thus becoming formed, but it seems probable that they are the commencing omphalo-mesaraic heart-rootlets.

Quite at the anterior end of this region the neural groove becomes abruptly shallow and then ceases. Just before its complete disappearance there is a folding or pitting inwards of all the layers (Plate X. fig. 13), but even here there is still no mesoblast at the axial part.

e. In the *region altogether anterior to the neural groove* the three layers are to be seen at the axis as elsewhere, the mesoblast having united across the middle line (Pl. X. fig. 14). A little way in front of the groove there is a slight thickening of the epiblast on each side, passing in more anterior sections into a median prominence, but this soon disappears, and the layers are smooth over the small remainder of the region covered by the amnion.

General considerations as to the relations of the blastodermic layers. Meaning of the primitive groove.

Professor His, in his large work on the development of the chick, described the two primary layers of the blastoderm—the epiblast and hypoblast—both before and also a short time after the formation of

the mesoblast, as closely united in the mesial line of the blastoderm into a longitudinal mass of cells (chiefly derived from the epiblast), to which he gave the name of *Axenstrang* (axis cord)[1]. It is this uniting mass running along the longitudinal axis of the blastoderm which, according to His, produces the appearance of a dim streak down the middle of the area pellucida, which has long been known as the primitive streak, but to which His applied the term *Axenstreif.* At a somewhat later stage, when the primitive groove has become formed along the centre of this streak in the posterior part of the blastoderm, it is seen that the *Axenstrang* is prolonged for a certain distance in front of the primitive groove. This prolongation is termed by His the anterior axial process (*Axenfortsatz*). As it is traced forwards the connexion between epiblast and hypoblast becomes severed, or, as stated by His, the *Axenstrang* becomes detached from the epiblast and continued into the central thickened part of the hypoblast.

The view of His, with regard to the union of epiblast and hypoblast in the middle line, has not been adopted by other observers, with the exception of Waldeyer[2]. The term *Axenstrang* has served, when used at all by others, to denote the part of the mesoblast which is fused in the middle line with the epiblast, or, as Kölliker puts it, the thickening of the axial epiblast from which the mesoblast is produced, and it has for the most part been altogether denied that the hypoblast takes any part in its production. An attempt has even been made to refer the observations of His as to the existence of a blending of the epi- and hypo-blast to faulty methods of preparation[3], but an argument of this sort can hardly be permitted easily to nullify the matter-of-fact statements of an experienced observer. For the rest, the illustrations given by His are obviously faithful representations of the objects, as Kölliker himself seems disposed to admit, and in this respect there is very little wanting in the clearness with which in some of the sections the blending of the epi- and hypo-blast in the *Axenstrang* is shown[4].

The prolongation of the primitive streak in front of the primitive groove (the *Axenfortsatz* of His) was observed first by Dursy, and has since been noticed more particularly by Waldeyer, Götte, and Kölliker[5]. By all it is regarded either as the anterior part of, or as a

[1] See also Rathke (quoted by His), *Entwickl. d. Wirbelthiere*, p. 20.

[2] Waldeyer, *Ueber d. Keimblätter u. d. Primitivstreifen bei der Entwickl. des Hühnerembryo*, *Zeitschr. f. rat. Med.* 1869.

[3] Kölliker (*loc. cit.* page 102) ascribes the results to the employment of osmic acid; whereas Balfour (*Quarterly Journal*, 1874, p. 341) lauds this reagent as showing in a distinct manner the line of separation between the two layers, and condemns chromic acid specimens, the examination of which "might possibly lead to the supposition that a structure similar to that which has been called the *axis-cord* was present."

[4] In some of the deductions drawn by His, the same confidence cannot so freely be placed as in his delineations; for example, in the statements as to the formation of the mesoblast, and as to the development of the protovertebræ, chorda and other parts from the *Axenstrang*.

[5] Götte, *Archiv f. Micr. Anat.* Vol. x. 1874; Dursy, *Der Primitivstreif des Hühnchens*, 1867; Kölliker, *loc. cit.* pp. 107, 135; Waldeyer, *loc. cit.*

growth forwards of, the primitive streak (or rather the thickening to which the appearance of a primitive streak is due), and the first three of the above-mentioned observers refer to it the production of the notochord (cephalic part, Waldeyer). Kölliker, on the other hand, who terms it the cephalic process (*Kopf-fortsatz*) of the primitive streak, is of opinion that it plays an important part in the formation of the head of the embryo, but is by no means clear with regard to its precise destination. He regards it as a part of the mesoblast, and, like the rest of that layer, a product of the primitive streak, but is compelled to admit that, as Götte's delineations also clearly show, it is differentiated off from the mesoblast on either side.

What then is to be inferred from a consideration of these various statements, especially with reference to the nature of the fused tract of axial epiblast and hypoblast in the guinea-pig embryo? It must, in the first place, be pointed out that His has confounded two distinct appearances under the name of *Axenstrang*, as a reference to his figures plainly shows. He applies the term both to the fusion of epiblast and hypoblast which first occurs, and to the fusion of epiblast and mesoblast which is represented as subsequently taking place. Other observers have confined the term to the latter condition, and have altogether denied the former. I have already given reasons why credence should be awarded also to the existence of this former condition. And the probability of such fusion at an early period is, in my opinion, strengthened by the existence of a similar condition in front of the primitive groove in the embryo here described.

Owing to the existence of this confusion of terms it is not easy to assign exact limits, either as regards time or place, to the occurrence of the two tracts of fusion respectively. If, as is most probable, the epi-hypoblastic fusion occurs *first*, the following may be taken to be the order of the early changes undergone by the blastoderm (starting with two distinct primary layers, epiblast and hypoblast). 1. Fusion of the two layers over a limited tract near the centre. 2. Thickening and depression of the epiblast behind this tract (primitive streak and groove) and (a little later) also in front of it (neural groove) 3. Lateral outgrowth of mesoblast from thickened epiblast of primitive groove. 4. Spreading of mesoblast over the whole blastoderm between epi- and hypo-blast (except underneath neural groove). If, on the other hand, the epi-hypoblastic fusion takes place at a subsequent stage the changes the blastoderm undergoes would be as follows:—1. Thickening and depression of epiblast along the middle line in the posterior part of the blastoderm (primitive streak and groove). 2. Lateral outgrowth of mesoblast from thickened epiblast of primitive groove. 3. Fusion of thickened epiblast with hypoblast at anterior part of primitive groove. 4. Redifferentiation of axial epiblast and hypoblast from the fused tissue, and formation of neural groove, the fusion and re-differentiation going on constantly from before backwards. According to Rathke, His, and Waldeyer, the epi-hypoblastic fusion exists from the beginning, but

this is doubtful[1], and it is also unlikely that it produces the whole of the primary axial shadow known as the primitive streak, as believed by His. For, at any rate, it is found that as soon as the primitive groove makes its appearance, the mass of cells which lies below the groove is a thickening of the epiblast, continuous on either side with commencing mesoblast (commencing mesoblast fused in the middle line with epiblast, as described by most authors), and has no connexion whatever with the hypoblast. But in the guinea-pig embryo, as we have seen, the deeper part of this axial thickening of the epiblast, which has always hitherto been regarded as either being (most authors) or forming (Kölliker) the axial portion of the mesoblast, can be seen, by tracing it forward in the sections, to be directly continued into the fused epi-hypoblastic tract, and this, traced still more anteriorly, becomes completely differentiated into epi- and hypo-blast, which, although quite distinct layers, are still in contact with one another at the axis, no trace of mesoblast coming between them.

Along the whole length of the axis of the embryo, except perhaps quite anteriorly and posteriorly, there is no trace of any tissue which can rightly be regarded as mesoblastic. Over a very limited tract, which may be termed for purposes of description the *centre of growth*, there is practically but one layer, for the epiblast and hypoblast are here inseparably connected. Both in front of and behind this centre a modification can be observed similar in character in both situations, in the splitting of the undivided mass into the two layers which are known as epiblast and hypoblast, and in the presence of a depression passing both anteriorly (neural groove) and posteriorly (primitive groove). It may further be brought to mind that, extending on either side from the centre of growth at right angles to these longitudinal grooves, there is sometimes to be seen, at a very early stage of development, when the blastoderm is still nearly circular, a *transverse furrow*[2], so that an appearance of radial symmetry is simulated by the blastoderm. It is true that this appearance soon vanishes in consequence of the greatly preponderating growth of the blastoderm along one of the axes, the longitudinal, and especially, in subsequent stages, along the part anterior to the transverse axis, but nevertheless the existence primarily of a radial symmetry in the blastoderm of the higher vertebrata, if not merely accidental, is of interest in a phylogenetic point of view[3].

The bilateral symmetry, which so early eclipses any other, appears to be essentially dependent on, or at all events contemporaneous in its appearance with, the development of the mesoblast. From isolated observations which at various times I have had opportunity to make on the chick, and, but in much rarer instances, on the mam-

[1] In the blastoderm of a cat-embryo (described by me in the *Proceedings of the Royal Society*, No. 168, 1875), which was still only bilaminar, both epi- and hypo-blast were quite distinct throughout their whole extent; and this accords with the statements of most other observers.

[2] See His *Entwickl. d. Hühnchens*, p. 65.

[3] The existence of such radial symmetry would so far militate against Hæckel's conception of the distinctiveness of the radial and bilateral types.

malian ovum, I had been led to the conclusion, even before the publication of the extensive researches of Kölliker on the subject, that the middle layer of the blastoderm, springs, in these classes of vertebrata at least, from the epiblast; and not merely by a simple thickening of the epiblast due to a proliferation of its axial cells, but, in the first instance, by an infolding of that layer, followed by proliferation of the cells at the bottom of the involution. The depression of epiblast is not seen as a groove because its sides are in close apposition; subsequently, by a widening out the primitive groove may be produced from it. So that the primitive groove would, on this supposition, represent an original involution of the epiblast which is connected with the origin of the mesoblast, and this involution occurs at a part of the blastoderm altogether posterior to that in which the embryo is produced. At the embryonic part (region of the neural groove) there is originally no mesoblast: this layer being produced as an outgrowth from the sides of the involuted proliferated epiblast which underlies the primitive groove (from the region of the primitive groove therefore), and it then rapidly grows forwards along either side of the longitudinal axis anterior to the primitive groove, spreading also at the same time behind and at the sides between the epi- and hypo-blast over the whole blastoderm. In front of the region of the neural groove, or, as we may equally well term it, the embryonic region, the lateral portions of mesoblast of either side meet and unite to form one sheet, whereas along the whole of the embryonic region they are completely separated by the contact with one another of epiblast and hypoblast. According to this view of the case the mesoblast does not enter primarily into the formation of the embryo, which is developed from the part of the blastoderm anterior to the transverse axis of the blastoderm, whereas the mesoblast is formed from the part posterior to this axis.

Another hypothesis has been put forward by Balfour[1] to account for the appearance of the primitive groove in Birds and Mammals, by a reference to the mode of development of Elasmobranch fishes. The embryo in these is situate at first at the edge of the blastoderm. "In the course of development the blastoderm grows round the yolk far more slowly in the region of the embryo than elsewhere. Owing to this the embryo becomes left in a bay, the two sides of which eventually meet and coalesce in a linear fashion immediately behind the embryo, thus removing the embryo from the edge of the blastoderm and forming behind it a linear streak not unlike the primitive groove. We would suggest the hypothesis that the primitive groove is a rudiment which gives the last indication of a change made by the Avian ancestors in their position in the blastoderm, like that made by Elasmobranch embryos when removed from the edge of the blastoderm and placed in a central situation similar to that of the embryo Bird......The central groove might probably also be viewed as the groove naturally left between the coalescing

[1] Review of Kölliker's *Entwicklungsgeschichte*, 2te Auflage. See this *Journal*, July, 1876.

edges of the blastoderm. Would the fusion of epiblast and mesoblast also receive its explanation on this hypothesis? We are of opinion that it would. At the edge of the blastoderm, which represents the blastopore mouth of Amphioxus, all the layers become fused together in the unamniotic Vertebrates. So that if the primitive groove is in reality a rudiment of the coalesced edges of the blastoderm we might naturally expect the layers to be fused there...."

This hypothesis is extremely ingenious, but there are serious objections to its acceptance. One of the most obvious of these is the difference in the time at which the structures respectively appear. The primitive groove is formed before the appearance of the embryo; whereas the linear streak of coalescence referred to by Balfour is not produced until the embryo has advanced considerably in development. We should moreover certainly expect to find a coalescence of hypoblast with the other layers under the primitive groove, whereas, according to the testimony of almost all observers, no such condition is ever present in this situation. Hensen's statements on this subject cannot be considered to outweigh those of all other observers. Moreover, we should expect to find the same condition at what is undoubtedly the edge of the blastoderm. And if we accept Kölliker's account of the origin of the mesoblast, and there can, we think, be little doubt that for Birds and Mammals at least this is in the main correct, the idea of a thickening and lateral *outgrowth* of the axial epiblast in the higher Vertebrates, representing a median *coalescence* of previously distinct halves or lateral portions of all the layers in Elasmobranchs, is scarcely tenable.

Mode of Connexion of the Ovum with the Uterus.

The pole of the ovum opposite to the embryo is firmly connected with the mucous membrane of the uterus. The lower part of the ovum is formed, it will be remembered, by only two layers of the blastoderm, the hypoblast and mesoblast, these enclosing, at the sides and below, the large cavity (Pl. XI. fig. 5, *m. c.*) which occupies the greater part of the ovum, and is bounded above by the amnion. The mesoblast is a single layer of flattened cells lining the vacuolated columnar cells of the hypoblast. But at the attachment to the uterus the two layers are separated from one another by an outgrowth of vascular tissue from the uterus, which has pierced the hypoblast in several places at the lowest part of the ovum, and has burrowed some little distance between the hypoblast and mesoblast. The condition of things will be readily understood by a reference to the diagram, Plate XI, fig. 5, which represents a longitudinal section through the whole ovum,

including the portion of the uterine wall to which it is attached. The mesoblast *m″* is seen to pass continuously over the vascular tissue above mentioned. The hypoblast *h*, which at the sides of the ovum is in close contact with the mesoblast, separates from it at the points *l l* in the section, and is continued outside the vascular growth, which is thus included between the two blastodermic layers. Where the lower surface of the ovum is in contact with the uterine wall the hypoblast is no longer seen as a single distinct layer. The epithelial cells here (fig. 7), lying that is between the vascular tissue *v. t.* above mentioned and the uterine mucous membrane *m. m.*, are two or three deep, are rounded in form, and appear to represent not only the layer of hypoblastic cells belonging to the ovum, but also the epithelium of the uterus, the two being more or less blended together. Here and there the more superficial of the cells in question approach in character to the hypoblastic cells elsewhere[1]. The vascular tissue, which is thus included between the blastodermic layers, is cavernous in structure, and obviously an outgrowth from the blood-vessels (veins) of the uterine mucous membrane. These veins (Plate XI, fig. 7, *v′*) are lined by thick, granular, epithelium-like cells; and similar cells, one or more layers deep, form the upper and lower boundaries of the cavernous tissue, and traverse it in the form of imperfect partitions. All the spaces of the tissue in question are seen in the sections to be filled with blood. Of its boundaries the upper one—that next to the mesoblastic layer—is the thicker, and in parts takes on quite the character of a columnar epithelium. This is especially marked near the growing border (Plate XI, fig. 6, *l*), where there is a continuous layer of such columnar cells *c* in contact with the mesoblast. At the place where the hypoblast and mesoblast separate this layer folds round and follows the hypoblast, its cells becoming gradually shorter and flatter, and coming into close contact with those of the hypoblast. In fact, from their appearance simply, it is not easy to make out a distinction between the two kinds of cells. At some parts of the border a clear space *s* is enclosed by the fold just mentioned. This space contains a

[1] It is possible that this resemblance may be accidental, and that the hypoblast is absent at this part.

few blood-corpuscles, but is nevertheless shut off from the rest of the cavernous tissue by a sort of plug *p* of densely packed cells, evidently proliferating. Some of those next the space appear to have become broken down: it is possible that the blood-corpuscles above mentioned have been produced within them. At other parts of the border the space is absent and the plug of proliferating cells is in immediate contact with the terminal fold.

Bischoff described the ovum of the guinea-pig as becoming invested by a *decidua reflexa*, which grows up around it, and eventually entirely encloses it in a new cavity distinct from that of the decidua vera. Reichert, on the other hand, stated, in opposition to Bischoff, that the ovum is invested merely by a prolongation of the uterine epithelium, which forms a sort of "capsule" for it, and that this capsule becomes excavated below the ovum into a hollow stalk, filled with fluid and containing the ovum at its extremity; thinking, quite erroneously, that the epiblastic or amniotic vesicle represented the whole ovum, and that the layer of cells covering the exterior of the ovum, described by Bischoff as the hypoblast (*vegetatives Blatt*), was nothing but such a prolongation of the uterine epithelium. Probably Reichert was led into this error by the occasional adhesion of the epithelium lining the decidua reflexa to the exterior of the ovum. But it seems difficult to understand how Hensen, with the aid and guidance of microscopic sections, could have adopted Reichert's view. There can be no doubt whatever, in contemplating the sections, that the whole of the spheroidal body here described is, as Bischoff thought, the ovum. And I have very little doubt that the mucous membrane which was torn off with forceps in exposing the ovum was Bischoff's *decidua reflexa*. That it was not merely an epithelial structure, but an investment formed by the whole mucous membrane, can be seen in some preparations where a portion still remains at the side, adhering to the outer layer (hypoblast) of the ovum. It seems almost as if Hensen, misled by Reichert's statements, had mistaken the hypoblast of the ovum for an "epithelial capsule" derived from the uterine epithelium, from which in fact at the lower pole of the ovum it becomes almost indistinguishable. And the layer of cells which he represents [1] as growing down on the inner side of the "epithelial capsule," and which he terms hypoblast (*Darmdrüsenblatt*), must be mesoblastic. The fact that there is a homogeneous limiting membrane between this layer and the cells outside it does not exclude the latter from forming part of the ovum, for even at a very early stage such membranes are found between the layers of the blastoderm [2].

[1] *Loc. cit.* fig. 75.

[2] Compare Hensen, *Op. cit.* p. 364, and Virch. *Arch.* Bd. 30, and Self, *loc. cit.*

DESCRIPTION OF THE PLATES.

PLATE X.

Figs. 1—14 represent a series of transverse sections of the guinea-pig embryo previously figured in surface view (Vol. x. Pl. xxx, fig. 2); the series passing from behind forwards.

Fig. 15 is a representation of the embryo in outline in order to indicate as nearly as possible, by numbered lines, the places with which these sections correspond.

In figures 1, 7, and 8, the whole of the amniotic vesicle is represented; in the others the amnion, and in some cases the lateral portions of the embryo proper, have been omitted to economise space. In nearly all the figures the different blastodermic layers are represented by differences of shading, and where any one layer is continuous or fused with another, such continuity is indicated by a blending of their respective shadings. But in figs. 7 and 8 the details of the structure have been filled in, and these figures serve therefore to show the actual appearance presented by the blastodermic layers. Figs. 7 and 8 are from photographs of the preparations; all the other figures were sketched with the aid of a camera lucida. The scale to which the drawings have been made is represented at the bottom of the Plate.

e. epiblast.
a. e. axial epiblast.
m. mesoblast.
m'. amniotic mesoblast.
m''. parietal mesoblast.
h. hypoblast.
a. h. axial hypoblast.
f. part where epiblast and hypoblast are fused together.
p. g. (in fig. 1) primitive groove.
n. g. neural or medullary groove.
n'. g'. (in fig. 7) rootlets of the neural groove.
sp. (in fig. 10) split appearing in mesoblast.
sp'. (in fig. 11) the same becoming a circular canal.
am. amnion.
e. v. epiblastic or amniotic vesicle.

In fig. 1 the primitive groove is seen. Opposite the groove the epiblast is considerably thickened, and this axial thickening of epiblast passes on either side continuously into the mesoblast, the hypoblast being quite distinct.

In figs. 2 and 3 the primitive groove is no longer seen. The relations of the layers are not materially altered.

In fig. 4 the axial thickening of epiblast is almost completely marked off from the mesoblast. The hypoblast is still distinct.

In fig. 5 the axial epiblast is united with the hypoblast.

In fig. 6 the union between epiblast and hypoblast is still observed, and the united part is somewhat broader.

In fig. 7 a line of demarcation is seen extending from either side between the axial epi- and hypo-blast, but the central cells are still common to both layers. The rootlets of the neural groove are seen.

In fig. 8 the neural groove itself is observed and opposite to it the epi- and hypo-blast are now quite distinct, although in contact with one another. They retain this relation in all the succeeding sections.

In figs. 9, 10, and 11, the neural groove becomes deeper and narrower, but in fig. 12 it has become much shallower preparatory to its complete termination.

In fig. 13 a pitting inwards of all the layers of the blastoderm is observed. There is still no mesoblast between the epiblast and hypoblast in the axis of the embryo, but in fig. 14 the mesoblast is seen between the two layers here as well as at the sides.

PLATE XI.

Fig. 1 represents under a high power and in detail the axial part of the section shown in fig. 5 of the preceding Plate. The references are the same as before.

Fig. 2 is taken from a section intermediate between those shown in figs. 6 and 7, Plate x. The nest *n* of small undifferentiated cells referred to in the text is seen in this figure; on either side of it a line of demarcation can be traced between epiblast and hypoblast.

Fig. 3 is the axial part of a section similar to that shown in fig. 9, Plate x. The columnar character of the cells of the axial hypoblast and the distinct line of demarcation between them and the axial epiblast is seen.

Fig. 4 is from near the anterior part of the neural region. The cells of the axial hypoblast are still somewhat columnar, and the small superadded cells (*a' h'*) referred to in the text are observed.

Fig. 5. Diagrammatic representation of a longitudinal section through the whole ovum along the axis of the embryo, and including the attachment to the uterus.

Most of the references are the same as before; the following are additional:—

m. c. general or mesoblastic cavity of the ovum.

all. allantois.

m. m. mucous membrane of uterus.

v. t. vascular or cavernous tissue connected with uterine mucous membrane at *m'. m'.*, and burrowing between the parietal mesoblast and hypoblast.

l, l. limits of uterine tissue.

s. clear space at growing edge of vascular tissue.

m''. m''. a solid fungiform projection from the uterine mucous membrane.

Fig. 6. Section at edge of vascular tissue showing the mesoblast *m''*, and hypoblast *h* separating to enclose this space, which is bounded by the layer of cells *c* and by the plug of densely packed cells *p*. The space is seen to contain blood-corpuscles.

Fig. 7. Section through the base of the ovum and the contiguous part of the uterine mucous membrane.

m''. mesoblast of ovum forming a continuous layer of flattened cells (spindle-shaped in section).

v. t. cavernous tissue.

bl. blood-corpuscles, within its spaces.

h'. layer of epithelial cells next to the cavernous tissue (? derived from hypoblast of ovum).

ep. deeper epithelial cells.

m. m. mucous membrane of uterus.

v'. one of the veins of the mucous membrane cut across.

ON THE PHYSIOLOGY OF THE DEHISCENCE OF THE FRUIT OF MOMORDICA ELATERIUM. By CHARLES J. F. YULE, M.A., *Fellow and Tutor of Magdalen College, Oxford.*

THE following short account of the dehiscence of the fruit of Momordica is rather incomplete, and is intended merely to bring the case before physiologists in order that it may be more thoroughly worked out. The experiments here described were performed in the Physiological Laboratory of Magdalen College upon fruit grown in the adjoining Physic Garden; as the experiments were not commenced till late in the season, they are necessarily incomplete, and doubtless future investigations will modify largely the conclusions herein arrived at. The very consistent investigations published by Professor Burdon Sanderson in the *Proc. Roy. Soc.* for Nov. 20, 1873, on the Electrical Phenomena accompanying irritation and contraction of the leaf of Dionea Muscipula appear to comprise nearly all that had been done about the electrical conditions of motile vegetable tissues, and seem to go straight to the root of the fundamental properties of protoplasm in its diverse forms of animal muscle and nerve as a superior limit, and vegetable "cell-contents" on the other.

Momordica Elaterium is a prostrate cucurbitaceous plant, its fruit is a pepo supported above the ground by a peduncle from four to six inches in length, from which it depends. It has a rough warty or shagreened exterior, is about two inches in length, and when ripe changes very little in colour, becoming slightly whiter at the poles. The dehiscence is effected by the separation from the peduncle, a hole about three or four millimeters is thus left, through which the seeds are expelled together with a quantity of green acrid pulp, the pepo at the same time becoming softer and undergoing a diminution in size to the amount of $\frac{1}{8}$ in. transverse diameter, and $\frac{1}{11}$ in. longitudinal (Dutrochet). The fruit explodes so vio

lently when ripe as to expel the seeds upwards of 15 feet in a vertical direction on detaching the peduncle; this detachment takes place on the slightest touch when the fruit is ripe, but even when it is very unripe there is a considerable tension of the contents, although the peduncle breaks across its substance rather than become detached in the regular way; in this case the experiment has to be performed by means of a knife.

The contractile action of Momordica Elaterium has been partially investigated by M. Dutrochet, and published in the year 1828[1], long before the higher branches of physiology had been developed, and he came to the conclusion that the action of the fruit in expelling its seeds was a veritable contraction, and gives an ingenious reason for the action depending on the endosmosis of the central fluid into the more dense contents of the cells surrounding the central pulp. This, however, differs essentially from the contraction of a muscle in that it is the liberation of a certain amount of energy all at once, and is comparable with the fall of a weight, or the release of a spring. After the act there seems to be no reserve of force such as there is in exhausted muscle; in short, it is rather the dehiscence of a fruit distended from internal pressure than a vital contraction.

In investigating the electrical conditions of Momordica, the fruit was gathered by cutting through the peduncle with a sharp knife a short distance below the fruit, leaving a bit of the peduncle to be used as a trigger; two patches of the rough skin were then shaved away, one near the middle of the fruit, and one at its distal end or breech; to these bare patches were applied non-polarizable electrodes constructed on the usual principle, but slightly modified in form. The galvanometer used was one of Sir W. Thomson's pattern, recently made by Messrs. Elliott, having a resistance of about 5500 ohms; it was generally used with the upper magnet rather low down in order to render it less sensitive, and also to make the needle swing quickly. The $\frac{1}{8}$ shunt was generally used.

After several trials of supports it was found that the best

[1] *Nouvelles Recherches sur l'Endosmose et l'Exmose.* Par M. Dutrochet. Ballière et Cie Paris, 1828.

plan was to hold the fruit against the inverted electrodes by hand, as its shrinking at the moment of dehiscence was apt to destroy the continuity. The galvanometer was read and registered every two seconds, and from these readings the curves in the plate were constructed, the vertical line representing the intensity of the current as indicated by the galvanometer scale, and the horizontal line being divided into parts each representing two seconds of time.

The general results arrived at are briefly these:

1st. The breech of the fruit was generally found to be positive to the centre, that is to say, a current set from the distal end through the galvanometer back to the centre, returning to the positive electrode through the substance of the fruit; sometimes the reverse was the case in the proportion of 2 : 13. This seems quite to contradict what one would expect from a muscle where the current, even after subdivision of the muscle, sets from any peripheral to any central point in its longitudinal surface. The ripeness of the fruit did not seem much to affect the direction and force of the current, which was of such force as generally to necessitate the use of the $\frac{1}{9}$ shunt.

2nd. At the moment of dehiscence there was a decided negative variation; this took place to a varying amount, and sometimes passed zero. The current, however, soon recovered itself, and very frequently became greater than before the dehiscence. In fact, I think that it might be accepted as the rule that the current was increased after the dehiscence as soon as the negative variation had passed off.

This negative variation certainly seems to point to an actual vital contraction; yet from the structure of the fruit it is difficult to conceive how such can take place. It would, however, be quite consistent with a purely mechanical explosion, the development of the reverse current being part of the products of the liberation of the energy imprisoned in the fruit, just as work certainly and heat probably is. I think it would be rash to assume any great amount of vital action until the subject has been better investigated.

The following are the galvanometer readings of five experiments; the sign + denotes a current from the breech

to the centre of the fruit, and – one in the reverse direction; the mark – on the right-hand side of the columns indicates the instant of dehiscence. In the appended Plate will be found some of these tables worked into curves.

IX.	X.	XI.	XII.	XIII.
280	70	70	+ 90	+ 40
280	70	70	100	40
280	80	70	100 –	40
280	80	70	80	40 –
280	80	70 –	50	0
280	80 –	60	0	– 40
280	90	50	– 20	50
280 –	90	60	0	30
200	90	80	+ 20	0
100	90	90	20	+ 20
100	100	100	50	30
150	120	130	70	50
200	180	150	80	60
250	200	200	80	70
250	220	250	100	80
260	220	250	100	80
270	230	250	110	90
270	270	250	110	100
270	280	250	120	100
280	300	250	120	100
280	300	280	130	110
	310	280	130	110
		280	130	120
		280	130	120
		300	140	130
		300	150	140
		300		150
		300		160
		300		150
		300		150
		300		150
				150
				160
				170
				170

P.S. These experiments were performed during the autumn of 1875, and the paper written at that time.

Fig. 1. No. XIII. Breech + ½ shunt, rather unripe, the mark off | indicates the moment of dehiscence.

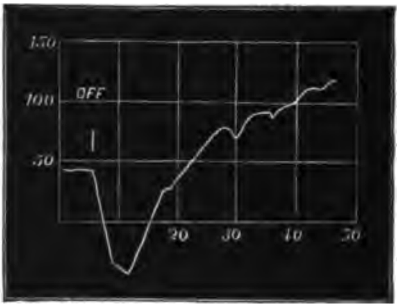


Fig. 2. No. XV. Breech + ½ shunt, unripe.

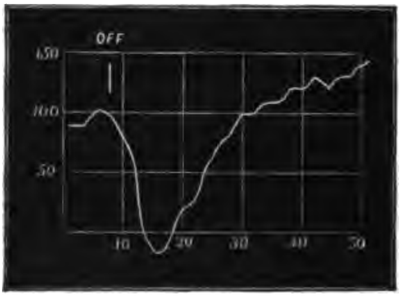
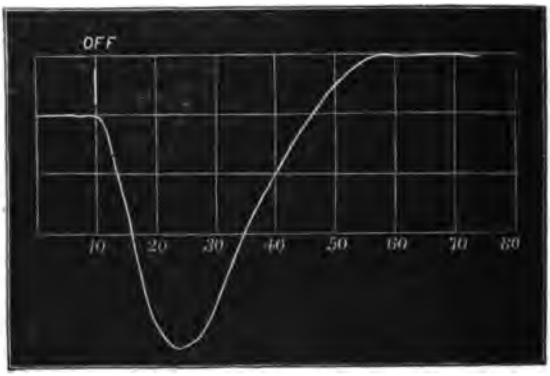


Fig. 3. No. VI. Breech + ½ shunt, quite ripe.



NOTE ON THE CASE OF ATROPHY OF RIGHT HEMISPHERE OF CEREBRUM, LEFT CEREBELLUM, &c., *published in the last volume by* H. A. CHATHAM GRAY, M.B. *Edin., Surgeon, Bengal Army.*

THE case recorded in Vol. X. p. 786, by Mr E. F. Brockman, of the Madras Medical College, has not been fully detailed; and as I was one of those who dissected the subject of this interesting lesion, I would like to render the case more complete.

While Mr Brockman notes the condition of the encephalon, he omits to mention anything about the spinal cord. This omission implies that it was normal. Further, he states that the left lung was much diminished in size, and that the other organs were normal. As Mr Brockman was not present at the dissection and *post-mortem* examination, he probably takes his notes from the Pathological Register, in which most cases are *very briefly* recorded. As far as I recollect the notes in the Register refer *chiefly* to the parts preserved in the Museum, and as only the encephalon was preserved, it is not likely that *full* notes of the case would be found in it. Dr Keess, the Professor of Anatomy, or Mr Richard Wilkins, F.R.C.S.E., the Curator of the Museum, both of whom were present at the examination, and took notes of the case, could have given full and correct information on the subject. Dr Keess expressed to me his intention of sending the brain and cranium to Dr Brown-Séquard.

I shall be brief in supplying these deficiencies.

(*a*) There was atrophy of the left half of spinal cord.

(*b*) The left spinal nerves were diminished in size.

(*c*) Left kidney and left ovary were smaller than their fellows.

(*d*) The left labium major and labium minor were atrophied.

(*e*) The blood-vessels on the left side were of smaller calibre than those on the right.

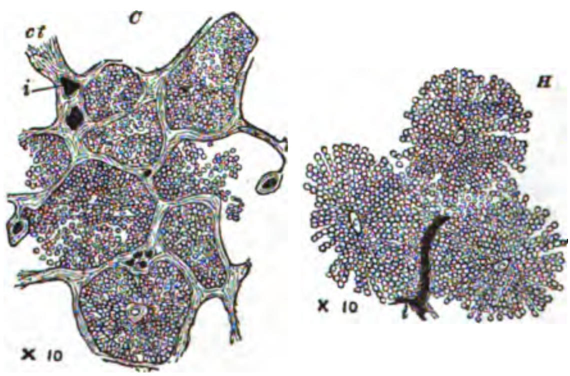
Mr Brockman says that nothing is known of the old woman's previous history. I remember Mr Wilkins making enquiries on this point, and the result being that the woman was a pauper, well known to the police, and that the policeman who escorted her body to the dissecting rooms stated that it was believed her mind was affected.

The case is exceedingly interesting and replete with instruction. It forcibly teaches the physiological doctrine that one half of the cerebrum is very closely structurally connected with the other half of the cerebellum and the body.

NOTE ON THE LOBULES AND THE CONNECTIVE TISSUE OF THE CAMEL'S LIVER. By PROFESSOR TURNER.

IN man, and the mammalia generally, the lobules of the liver are imperfectly separated from each other by the inter-lobular vessels and duct, and a scarcely appreciable quantity of areolar connective tissue. In the pig, as is well known, each lobule is circumscribed by a definite capsule of connective tissue. In the polar bear, Johannes Müller observed the lobules to be distinct and easily separable from each other, and a similar distinctness of the lobules has been seen by Hyrtl in the liver of the South American Rodent, *Octodon Cumingii.*

In the Anatomical Museum of the University of Edinburgh is a portion of the liver of a camel, imperfectly injected from the hepatic vein with size and vermilion, which was mounted some 30 years ago by my immediate predecessor, the late Prof. Goodsir. This specimen was always shown by him when lecturing on the liver to his class, as exhibiting, in even a more striking manner than the pig, evidence of the division of the substance of the liver into lobules by intermediate connective tissue. As no description of the relation of the connective tissue to the lobules of the camel's liver has ever been published, either by Prof. Goodsir, or any other anatomist, I propose to relate some observations which I have recently made on this specimen.



C. section through lobules of the camel's liver to show the capsules of connective tissue, *ct.* *i.* divided inter-lobular vessels. By way of comparison a similar section through the human liver *H* is given. *i.* inter-lobular vein with a slight sheath of connective tissue. *c.* central vein of lobule.

The peritoneal surface of the liver was in part smooth, and in part divided by furrows into numerous irregular lobelets, which

varied in size from $\frac{3}{10}$ths of an inch to $1\frac{1}{2}$ inch in diameter. The free surface, both of these lobelets and of the undivided surface of the liver, was mapped out into multitudes of definite polygonal lobules, the outlines of which were marked by intermediate depressions. When sections were made through the substance of the liver, the surface of section presented a similar distinct lobular subdivision. The lobules varied in diameter from $\frac{1}{20}$th to $\frac{3}{20}$ths of an inch, and showed many slight variations in form.

The fibrous coat of the liver was tough, and closely adherent to the outer surface of the organ. When it was carefully dissected away, very distinct septa of fibrous membrane could be seen to pass from its deep surface into the substance of the liver, to become continuous with the connective-tissue capsules of the lobules. As the part of the liver in the region of the portal fissure had not been preserved, I am not in a position to state the arrangement of Glisson's capsule at that fissure; but throughout the substance of the organ, wherever a portal canal was divided, the portal vein and accompanying structures were seen to be enveloped by a comparatively strong sheath of connective tissue, which was continuous with the capsules of the adjacent lobules.

The coat of the hepatic vein was thicker than that of the corresponding vein in the human liver, and it was so loosely attached by connective tissue to the lobules which surrounded it, that it could be readily isolated by tearing through the areolar tissue, which passed from its outer wall to become continuous with the capsules of the lobules.

Each hepatic lobule was invested by a capsule of connective tissue, which was so distinct as to be readily recognised by the naked eye, but the capsules of adjacent lobules were blended with each other. This capsule was not of uniform thickness, but was thinner where it lay in contact with the sides of a lobule, than at the angles where three or four lobules came into relation with each other.

Fragment of the capsule of a lobule. *ct.* its connective tissue. *ct'.* intralobular prolongations of the connective tissue between the columns of cells.

The inter-lobular vessels were imbedded in the connective tissue

of the capsules of adjacent lobules. From the capsule of a lobule slender bars of the connective tissue, of microscopic dimensions, were prolonged into the interior of the lobule, in which they could be traced for some distance, extending towards the centre of the lobule between the columns of secreting cells.

It was further observed that whilst the intra-lobular bars near the periphery of the lobule had, like the capsule, the fibrillated character of areolar tissue, as they approached the central region they had a very delicate membrane-like structure. In the peripheral part of the lobule the presence of a sustentacular connective-tissue framework, quite distinct from the network of capillary blood-vessels, could be demonstrated without difficulty; but in the more central part of the lobule, it was not possible for me, in the condition of the specimen, to state precisely if the membrane-like structure was distinct from, or blended with, the wall of the capillaries. I was unable also to determine whether any relation existed between this framework and the inter-lobular branches of the hepatic duct, or the intra-lobular biliary passages. Though these notes are imperfect therefore in these particulars, they may serve to direct the attention of observers who may have the opportunity of examining fresh specimens, to the liver of the camel as an organ which, from the great development of the framework of connective tissue, deserves to be more thoroughly investigated.

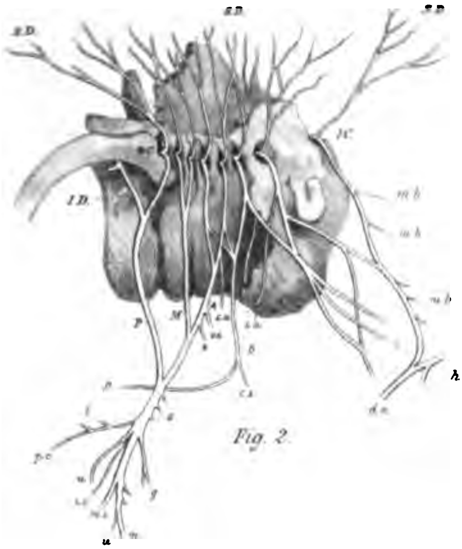


Fig. 2.

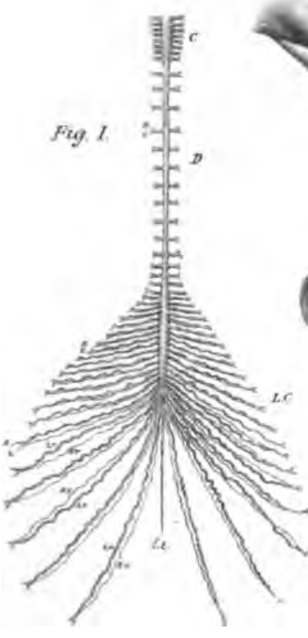


Fig. 1.

Fig. 3.

Fig. 4.

J. H. Scott, M.B. delt   F. Huth, Lithr Edin

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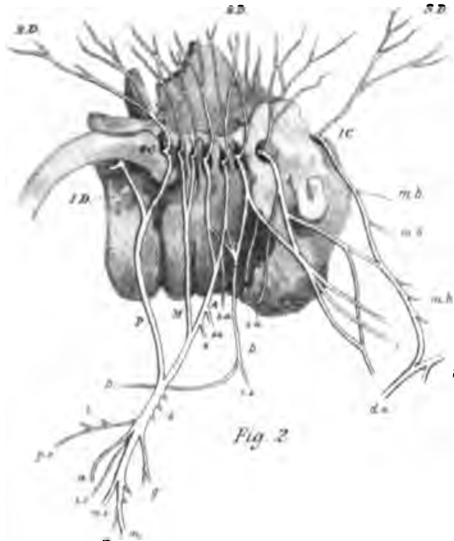

Fig. 2.

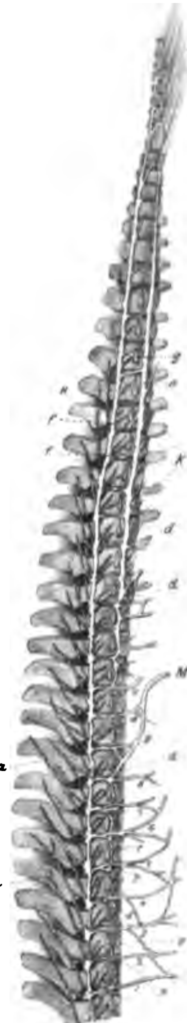

Fig. 4.

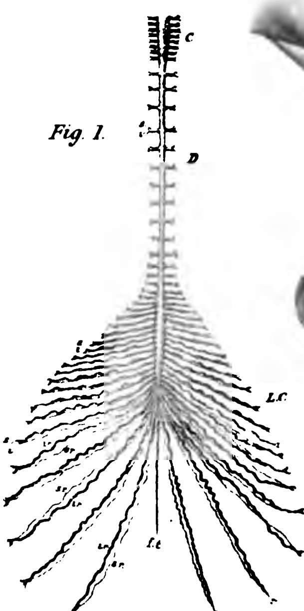

Fig. 1.

Fig. 3.

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Journal of Anatomy and Physiology.

A CONTRIBUTION TO THE MINUTE ANATOMY OF THE HUMAN RETINA. By R. Marcus Gunn, M.A., M.B. (Edin.). (Plate xii.)

[From the *Physiological Laboratory, University College, London.*]

(See Note and Explanation of Plate, p. 516.)

The object of the present paper is to describe an apparently direct connection between the cones of the retina and certain of the corpuscles of the inner nuclear (granule) layer. It will be useful to preface the description by giving a short explanation of some of the terms employed.

The rods and cones, seated on the *limitans externa*, are each prolonged by a straight fibre—finer in the case of the rods than in that of the cones—which passes directly through the external nuclear ("granule") layer (one of the granules of which is interpolated in the course) as far as the external molecular (intergranular) layer. Having attained the outer surface of this layer each fibre ends in a well-marked enlargement, which may be termed the rod-fibre enlargement, or the cone-fibre enlargement, as the case may be; or, more shortly, the bulb of the rod- or cone-fibre. The bulbs of the rod-fibres seem like exaggerations of the minute varicosities these fibres exhibit at intervals along their course, and they have a rounded or oval shape. The bulbs of the cone-fibres, on the other hand, are larger and much better characterized. Their shape is pyramidal with the base resting on the external molecular layer; and from the basal margin various observers have described fine fibres extending a short distance into and becoming lost in that layer.

Of the elements to be found in the internal nuclear (granule) layer at least three or four distinct kinds have been described.

Those which are the most numerous, and of which alone we shall have occasion to speak, are bipolar cells with the one process—the outer—extending outwards towards and into the external molecular layer, and the other process—the inner—passing inwards into the substance of the internal molecular layer. Into the internal molecular layer extend also the branching processes of the cells of the ganglionic layer, tending towards the internal nuclear layer.

It has generally been believed, by Max Schultze and most of the recent writers on the retina, that a connection exists between the ganglion-cell-processes and the inner processes of the internal "granules" on the one hand, and between the outer processes of the internal "granules" and the rod- and cone-fibres on the other; but this connection has always been assumed to take place through the medium of a network of numerous and exquisitely fine fibrils, derived from the branching of the fibres and cell-processes above referred to, and seated in the outer and inner molecular layers respectively.

From the study of sections of the human retina prepared with osmic acid, and subsequently hardened in alcohol, I have been able to convince myself that a far more direct connection than that hitherto conjectured, subsists between the outer processes of some of the internal "granules" and the terminal enlargements or bulbs of the cone-fibres. It has in fact been possible, in numerous instances, to trace the outer process of one of the granules in question through the external molecular layer immediately into the bulb of a cone-fibre (Plate XII. Figs. 2—6). The connecting fibre, which is often tapering, generally passes to one of the edges of the bulb. It is sometimes comparatively broad and ill-defined (Fig. 4), at other times finer but much more distinct, and may then take a somewhat wavy course (Fig. 2), and have a more oblique direction; but it is possible that these differences of appearance depend upon the aspect from which the connecting fibre happens to be viewed. Occasionally, but rarely, the bulb of a cone-fibre has seemed to receive two such processes, one at either side (*Stu*, Fig. 4), and it is not unlikely that this may be the normal state of the case in all, the second connection having been severed in making the sections.

In some instances (perhaps in every case) the outer process of the inner "granule" bifurcates close to or within the substance of the external molecular layer[1], and it has occasionally been possible to follow one at least of the resulting branches into the bulb of a cone-fibre in the manner above described. Whether the other branch ends in the bulb of another cone-fibre I have been unable to determine. In one case at least it appeared to divide again into two or three very fine branches, and these seemed rather to tend towards the bulbs of adjacent rod-fibres, but a connection with them could not be distinctly perceived: if it exists at all it must be of excessive delicacy.

Lastly, I would mention that in a solitary instance I observed what appeared to be a direct continuation of a branch of one of the ganglion-cells of the ganglionic layer into the inner end of one of the internal "granules" (Fig. 3); this, on the other hand, by its outer process was in connection with the bulb (*d*) of a cone-fibre, in the manner above described. At the same time I am not prepared to lay too much stress on this observation. For in the first place it is, as just mentioned, solitary; and secondly, by the method of preparation adopted, the ganglion-cells and their processes exhibit nearly the same, or, if anything, a rather less amount of staining than the substance of the internal molecular layer in which they are embedded; and this fact renders the course of their branches very much more difficult to trace.

It was found possible to obtain sections of retina of the extreme thinness requisite for such an investigation as the present only by the employment of the cacao-butter method of embedding[2]. The chief difficulty otherwise experienced was in making the plane of section exactly vertical to the surfaces and corresponding with the direction of inclination of the fibres in the retina. The connections described were investigated with the highest obtainable power[3].

[1] Occasionally, as Mr Hulke has shown, instead of a single bifurcating outer process two separate fibres are observed to pass in an outward direction from one of the inner granules.

[2] See Mr Schäfer's description in this *Journal*, Vol. x. p. 775.

[3] The no. 12 immersion of Hartnack was the objective mostly used for this purpose.

ON THE CHANGES OF THE BLOOD-STREAM IN MUSCLES THROUGH STIMULATION OF THEIR NERVES. By W. H. GASKELL, M.A. (Plates XIII. and XIV.)

AN observation of Sczelkow[1] caused Sadler[2] to estimate the rapidity of the outflow of blood from the open vein of a muscle, before, during and after the tetanus of the latter. His experiments show, with absolute certainty, that stimulation of a muscle-nerve, at the same time that it causes a shortening of the muscular fibres, produces a considerable effect upon the blood-flow through the vessels of the muscle, the flow in fact being quickened. It was not, however, possible by means of Sadler's method of experimentation, to represent at all accurately the relations between the changes in the form of the muscle and in the rate of the blood-stream from time to time, a circumstance which was probably the essential reason why he did not succeed in coming to any positive conclusion as to the cause of the quickening of the stream. Since, however, the present means at our disposal enable us to fill up the gaps in his observations, I, at the suggestion of Prof. Ludwig, of Leipzig, again took up the subject.

My method of experimentation agreed with Sadler's so far, that I too measured the amount of blood flowing out of the vein of a muscle before, during, and after the contraction of the same. In other respects, however, it differed from former methods so widely, that I feel obliged to give a more detailed description of it.

Instead of the biceps femoris muscle I used in the majority of cases the quadriceps extensor group of muscles, the vein used being that one which collects the main part of the blood from the vasti and crureus muscles, see Pl. XIII. vi. Since this vessel receives in addition only a moderately sized branch from the gluteus, and, close to this, a very small branch from the skin on the outer side of the trochanter, it is essentially a

[1] *Wiener Akad. Sitzungsberichte*, 45. Bd.
[2] *Arbeiten aus der phys. Anstalt zu Leipzig*, 1869.

muscle-vein. Near its mouth, often in fact united with it, a second branch opens into the femoral vein, which too receives its blood from the anterior parts of the thigh, see Pl. XIII. vii. This second branch, which collects the blood of the rectus, sartorius, and tensor-vaginæ-fasciæ muscles, receives also a considerable supply from the skin covering those muscles. Therefore this division of the so-called anterior thigh-vein was intended not to be used; however, in consequence of the intimate connection of the two branches and their gradual origin from their sources, it was not possible to predict beforehand the limits of the muscular tract made use of. This was, therefore, always determined by subsequent dissection, the result of which I can here assert to be, that in all cases the sources of the blood-stream under observation were most preponderatingly the three great muscles, vastus-internus, vastus-externus and crureus.

In order to prepare this vein, which we may call for short the extensor vein, for our experiment and especially to make sure that the blood collected came only from the above-mentioned muscles, I proceeded as follows, after the fashion shown in Pl. XIII. The trunk of the femoral vein was laid bare by means of a sufficiently long incision in the skin, beginning straight over Poupart's ligament, carefully freed from connective tissue with blunt instruments, and ligatured in the middle of its course along the thigh. Then all the other veins that empty themselves into the femoral between the middle of the thigh and Poupart's ligament were tied, with the exception of what I have called the extensor vein. Two strong threads were now placed under the femoral, at a distance of one to two centimeters above and below the mouth of the extensor vein respectively, Pl. XIII. SI, SII. The lower thread SII was then tied round the femoral in a slip-knot, and the vein itself opened at a suitable distance below this ligature. Before the canula, which I shall shortly describe, was inserted into this opening, I made certain whether or no a valve existed between the mouth of the extensor vein and this opening; its presence was easily proved by loosening the slip-knot round the femoral below the extensor vein, and at the same time lifting the upper ligature until the lumen of the femoral was closed. If

the blood did not then flow out of the opening below the extensor vein in a full stream, the obstruction in the shape of a valve was broken down by means of some blunt instrument. This operation was necessary only once or twice. As soon as it was clear that there was no obstruction here, the lower of the two threads SII was again tied in a slip-knot, and at the same time the upper closure of the main venous trunk removed.

The canula that was used consisted, as Fig. 2 on Pl. XIV. shows, of two tubes made of German-silver, fitting into one another, the one ⊥-shaped (*a*), and the other a tube bent at right angles (*b*), with its shorter arm drawn to a fine point. These two tubes were fixed together, so that the shorter arm of the bent tube, which stood horizontal during the experiment, was tightly fixed into the short limb of the ⊥-shaped tube. By this arrangement, as the figure shows, there was a space left between the two portions of the tubes that were inserted into each other; and, therefore, it was possible for a fluid, pressing towards the open mouth of the horizontal arm of the ⊥-tube, to find its way at the same time through the vertical limbs of the ⊥ and the bent-tube. In order conveniently to separate the two tubes from one another, we will call the ⊥-tube the "blood-canula," and the bent tube the "wash-canula."

The two canulæ, made out of glass or German-silver, were tied into the opening in the femoral vein, with their mouths directed towards the abdomen, Pl. XIII. *c*. In consequence of the nature of the spot chosen, it was possible at will to turn the flow of blood from the extensor vein either into its natural direction towards the heart, or else into the canula, without checking the blood-flow out of the muscles for a single moment. By lifting the upper ligature-thread, after having loosened the lower slip-knot, the stream was turned towards the canula, whilst by reversing the action, the blood flowed on towards the heart. At no time, therefore, was the blood forced back into the veins, so that not only was it possible to commence the measuring of the outflow at any point one chose, but also there was the great advantage, that the elasticity and irritability of the walls of the vessels were not affected, as according to my experience is quickly the case, when the blood stagnates in the muscle, owing to a stoppage of the vein.

The nature of the canula allowed of a more effective use of the washing-out apparatus which Sadler used. This latter consists, as Fig. 1 on Pl. XIV. shows, of a globe *a* filled with a solution of carbonate of soda, which poured out through the indiarubber tube *b c b* into the vertical arm *d* of the wash-canula, whenever the position of the cock *c* permitted it. This washing-out apparatus was naturally only put into action, after the femoral vein had been closed by the ligature between the canula and the opening of the extensor vein. When this had been done and the cock *c* left open, the carbonate of soda solution flowing out of the mouth of the wash-canula was able to pass into the stump of the vein, and from thence into the vertical limb *e* of the blood-canula. Since the manipulation necessary for this could be effected easily and quickly, one could always convince oneself of the absence of a clot, or get rid of one when present. In none of the experiments therefore, which form the basis of the following communication, is there the slightest suspicion of any error due to a clotting of the blood. Also the way the canula is inserted, in consequence of which there is never any interruption of the stream out of the muscles, still further obviates this objection, for, owing to this arrangement, there can never be any danger of a clotting of the contents of the extensor vein; and therefore, if there is no clot present between its opening into the femoral and the point of insertion of the canula, there can also be no clot in the whole tract of the experiment.

When the amount of blood coming out of the extensor vein was to be measured, the cock *c* was shut, the slip-knot SII below the extensor vein opened, and the thread SI above it tightened. The blood immediately gushing out of the vein passed through the limb *e* of the canula and from there reached the flask *f*, which was filled with a solution of carbonate of soda, forcing out of it a corresponding portion of its contents, which passed through the indiarubber tube *g* to the glass bent tube *h*. From the mouth of this, which was directed downwards and which stood some few millimeters below the level of the vein, the fluid poured into the wider limb of the U-shaped tube *i k l* and raised the marker which floated in the narrower limb. This marker recorded in the usual way all

variations of position upon a roll of paper moving with known rapidity in front of its pen. In order to suit this apparatus to the volume of the blood-flow, two tubes *i* and *m* of different diameters were fixed on that end of the U-shaped apparatus, which was turned towards the animal, either of which could be cut off at pleasure from the connection with the narrow tube. In the case of small dogs the blood was conducted into the narrower tube *i* throughout the whole course of the experiment. When this was used a volume of 0·35 c.cm. corresponded to a rise of one millimeter of the marker. In the case of larger animals the tube *m* was used at the beginning of the experiment; in this case a rise of one millimeter of the marker corresponded to 0·52 c.cm. of fluid. If the larger animal in the course of the experiment had suffered a considerable loss of blood, then the wide tube was changed for the narrow one. In order to be able to empty the measure-glass quickly, there was added to the horizontal limb of the U-tube an outflow opening *u*, which could be closed by a clip. If in the course of the experiment so much blood became mixed up with the contents of the flask *f*, that there was reason to fear the formation of clots in it, it was necessary to renew the carbonate of soda, which was easy to do by using an indiarubber stopper, with which to close the flask.

By means of the above-described method, the amount flowing out will it is evident be estimated accurately, but the moment of time of the outflow from the vein and the rise of fluid in the tube carrying the pen will not exactly correspond, owing to the indiarubber tubing inserted between the two. I make this remark rather to obviate the charge of an oversight, than because I imagined that such a slight disagreement in the correspondence of the time could constitute a noteworthy error in the experiment.

The nerves which supply the vasti and crureus muscles run, as is known, in the trunk of the crural nerve, which is easy to find underneath Poupart's ligament on the outer side of the ileo-psoas muscle, see Pl. XIII. *n*. After the nerve had been found, the electrodes imbedded in gutta-percha were placed round it, either before or after section of the same. The stimulation of the nerve by means of the interrupted

current commenced every time, after the nerve had first been cut and fixed by means of a thread to the cover of the electrodes. In order during the course of the experiment to be certain about the position of the electrodes, their gutta-percha casing was firmly sewed to the skin, and the wound that was necessary for the laying bare of the nerve, carefully sewed up.

The tract, which this nerve supplies, does not exactly correspond with that, from which the vein that is used takes its origin; for our vein collects a small part of its blood from the glutei as well. Undoubtedly the accuracy of a comparison between the amount of blood flowing out of the muscle masses, when at rest and when in action, is influenced in consequence. That however the value of the conclusions arrived at in the following pages is not damaged thereby, is clearly shown in the course of the paper. For its intention is, not to find out the absolute amount of blood which has flowed in a unit of time through a given muscle at rest, or in action, or just after action; and it is only the value of this estimate that can be influenced by the want of correspondence between the tract supplied by the nerve and that of the vein. On the other hand, the time at which any change in the blood-stream occurs cannot be affected.

Lastly, to complete my remarks about the method of preparation, it is only necessary to add, that all the animals experimented on with the exception of a single one were not under the influence of any poison; that the beginning and end of the nerve-stimulation was marked below the marker of the float on the roll of paper, and that sometimes the arterial pressure was estimated by means of a manometer. At the end of the experiment then, there was traced on the roll of paper, the time in seconds, the duration of the stimulation, and the variations of the rate of outflow of the blood from time to time. This latter was represented by a curve ascending with different degrees of steepness. In order from this curve to obtain an expression in numbers of the variations in the rate of flow, lines were drawn through it at intervals corresponding to five seconds, at right angles to the abscissa of the curve, and the heights of these ordinates measured. The difference between the lengths of two consecutive ordinates

gave a means of estimating the amount of blood that had poured out in this time, while, as already mentioned, the rise of a millimeter corresponded to either 0·52, or 0·35 c.cm. of blood. For convenience sake, another series of curves was constructed from the numbers so obtained, in which the ordinates represent the mean rate of flow for every five seconds. If however, as often happens, the rate alters in different directions during the course of five seconds, and therefore, if one were to take a mean value for the rate during this particular five seconds, essential peculiarities of the observation would be omitted, this particular period was again divided up into periods corresponding to the variations of the rate. In order to obtain ordinates for the amounts of this outflow, which was measured for a shorter time, that should be of the same value as the others, each one was calculated at the rate of five seconds duration.

Since it is possible to conduct the blood out of the vein into the measure-glass for longer than sixty seconds at a time without having to fear clotting, one obtains a continuous tracing of the outflow before, during, and after the tetanus. Now, even though for the whole of this time the blood is flowing out through the canula, still it is impossible to continue the tracing without interruption in those cases, where the capacity of the measure-glass is not great enough to hold the whole amount of blood poured out. Since, however, owing to the arrangement I have described above, one can empty the measure-glasses without interrupting the inflow to them, the experiment is not disturbed, and the length of time during which the tracing is missing is always quite short; and, if it happens that no sudden changes of rate occur during this time, it is easy to interpolate the gaps in the curve. In the woodcuts illustrating this paper, the interpolated pieces are distinguished by a dotted line.

1. The stream through the muscles at rest with nerve uncut.—Safe conclusions about the variations in the blood-stream through a muscle during its excitation and exhaustion can only be drawn, if there is a regular steady outflow when its fibres are at rest. One must, therefore, above all be sure of this fact.

Supposing that one leaves the nerve either before or after section absolutely untouched, and that the animal throughout remains quiet, then, as a matter of fact, the stream from the vein flows with nearly absolute regularity. In order to give the reader an idea of the strength of the flow, I insert the following series of figures, to which I would remark, that the animals which furnished them remained quite quiet during the experiment, and that the crural nerve was uninjured.

Weight of the animal.	Outflow for every 5 sec. in c.cm. Maximum.	Minimum.	Mean.	Duration of the obs.	Remarks.
12·8 kilo.	3·64	1·95	2·43	75 sec.	The variations follow quite irregularly.
9·4 "	2·17	0·95	1·39	65 "	The rate of flow diminishes with the duration of the experiment.
22·5 "	2·86	1·82	2·37	40 "	The variations follow irregularly.
16·4 "	1·30	0·90	1·04	25 "	The rate of flow diminishes with the duration of the experiment.
9·9 "	1·95	1·17	1·46	25 "	Curare. The rate diminishes with the duration of the experiment.
20·0 "	0·91	0·52	0·61	60 "	The variations follow irregularly.
?	1·56	1·04	1·23	40 "	The variations follow without regularity.

These figures show no greater variations than are also observed in other organs, where the vessels are situated in a less moveable substance. It is noteworthy, that the same, or at least approximate values return, after any interference whatever has driven the strength of the stream far out of its original limits. This naturally holds good, only when the loss of blood has not been too great in comparison with the whole amount which the animal originally possessed, and when also a pause of some few minutes has elapsed between the influence that has altered the flow and the renewal of the measuring.

In the above series of figures it often happens, that the rate of outflow diminishes with the duration of the experiment.

We shall meet with a similar occurrence later on, following upon the section of the nerve. If, after the strength of the blood-flow through the canula has markedly diminished, one turns the latter again into its natural course, and then, after it has streamed for five to ten minutes towards the heart, diverts it a second time into the canula, it often happens that it again flows at its original rate. This again diminishes with the duration of the experiment as in the former case. One might attribute this peculiar occurrence to the smaller resistance met by the flow through the canula and in consequence to the muscle emptying itself of a stored-up supply of blood, if there were not many arguments that could be raised up against this hypothesis. Among others, besides the inconstancy of the occurrence, I reckon the fact, that the original velocity does not return when the stream has flowed in the normal direction for only one or two minutes, a time, which must surely have been long enough for the vessels of the muscle to have again approximated to their original degree of fulness. The true reason for the phenomenon remains unknown to me.

2. The variations in the stream in consequence of section of the nerve.—The section of the nerves which supply the muscles under observation acts upon their blood-stream in a peculiar manner, about which Sadler has given us some information. I can amplify his observations in many points, since I have repeatedly succeeded in cutting the nerve, without interrupting the measurements of the outflow, which had already lasted some time. The phenomena, which occur after the section, ought naturally to be attributed to that only, or at least essentially, when that operation has been performed so quickly and cleanly, that only a temporary contraction of the muscle is caused and no symptoms of a painful sensation. I will now detail more fully one of the three observations, which have succeeded under these conditions.

Nerve uninjured; there flowed out every 5 seconds

0 to 5	5—10	—15	—20	—25	—30	—35	—40 seconds.
2·9	2·9	1·8	2·0	2·3	2·5	2·6	2·6 mean for 5 sec. 2·4 c.cm.

The nerve was cut, the muscles contracted slightly and temporarily; signs of pain entirely absent. The measurement of the outflow, which continued without interruption, gave for every 5 seconds

0 to 5	5—10	—15	20—25	—30	45—50	—55	—60	—65	—70	—75 sec.
4·4	6·0	8·0	14·6	12·2	9·5	8·7	7·3	6·5	6·2	3·6 c.cm.

During the time from the 15 to the 20 seconds, and from the 30 to the 45 seconds, the outflow through the canula continued but could not be measured.

After the outflow through the canula had lasted for 75 seconds since the section, the blood-stream was turned, for the space of a minute, towards the heart, and in the meanwhile the canula and the stump of the vein up to the lower ligature was washed out with carbonate of soda.

The flow from the canula commenced anew 135 seconds after the section of the nerve, and there streamed out every 5 seconds

135 to 140	—145	—150 seconds.
2·5	2·3	2·3 c.cm.

Up to this point the animal had lost 157 c.cm. of blood, that is, about 0·7 per cent. of his body weight. The mean pressure in the carotis was 156 mm. hg.

After the blood-stream had now flowed on in the direction of the heart for 12 minutes, it was again let run through the canula, and there flowed out every 5 seconds

0 to 5	—10	—15	—20	—25	—30	—35 seconds.
6·1	5·1	5·1	4·3	4·0	3·6	3·6 c.cm.

The possible presence of a clot was now put to the proof, and the washing out of the canula showed no trace of one.

We see then, that the outflow altered after the section of the nerve in such a manner, that it increased very quickly in rapidity during the first 20 seconds, until the amount had reached 6 times that given out when the nerve was uninjured. After this maximum rate was reached, it sank in the course of a minute to near its value before the section of the nerve. This latter operation then caused a temporary quickening of the stream. In the above experiment, the section of the nerve appears to have a lasting effect as well as a temporary one, for,

14 minutes after the section, the blood still flowed more fully than before that operation, though decidedly slower than during the first 30 seconds after the same. In one other of the three above-mentioned cases, precisely what I have described occurs again, while in the third, there is this difference, that the stream, which was considerably augmented shortly after the section, gradually returned again to the exact strength which it possessed before the nerve was touched. In this case then, only the temporary and not the lasting quickening of the stream was manifested. The following figures show this.

Nerve uninjured; there flowed out every 5 seconds

0 to 5	—10	—15	—20	—25	—30	45—50	—55	—60	—65	—70 seconds.
2·5	2·3	2·2	2·2	2·0	2·2	2·3	2·7	3·6	2·5	2·2 mean for 5 sec. 2·4 c.cm.

The nerve was cut, the muscles contracted feebly; no signs of pain. The measurement of the outflow, which continued without interruption during the section, gave for every 5 seconds

0 to 5	—10	—15	—20	—25	—30	—35 seconds.
1·6	10·1	9·2	7·0	4·4	3·8	3·3 c.cm.

After the outflow had continued through the canula for 110 seconds and 81 c.cm. of blood = 0·6 per cent. of body weight had been expended, the blood-stream out of the muscle was directed towards the heart. After the stream had now lasted 10 minutes in the normal direction, and the mean pressure in the carotis was found to be 122 mm. hg., the outflow through the canula recommenced, and gave in

0 to 5	—10 seconds.
2·3	2·2 c.cm.

Results similar to these, though naturally not so fully detailed, appear whenever the measurement of the blood-flow, immediately before and after the section, was unavoidably interrupted for some 30 seconds, supposing only, that the animal had not been too unquiet during the manipulation preparatory to this operation. All the observations which were made in this manner, show quite clearly the great temporary increase of flow, while the lesser, but more enduring rise, is manifest in some, but is wanting in others.

In seeking after the cause of the strong temporary increase of flow, it is possible to attribute it either to a direct action of the nerves on the vessels of the muscles, or to a secondary action effected by the contracting muscle-mass on the walls of the vessels. In agreement with Sadler, I must confess, that such a passing contraction as is caused by the mere section of the nerve, seems to me to afford no sufficient ground for such a marked swelling of the blood-flow. Of this we shall be more clearly convinced later on, when we consider the magnitude of the increase of flow produced by the contraction and tetanus of the muscles. If instead of this, we suppose a direct relation between the nerves and the vessel-wall, it is possible then for the effect to be due to the excitation of nerve-fibres, which are of the nature of vaso-dilatator fibres. This theory is consistent with an increased rate of flow, lasting a limited number of seconds, and followed by a diminution of the same. If, however, the cut acts as a stimulus to the dilatator nerves, a second cut must necessarily produce the same effect. Upon performing this experiment, the following was the result.

Before the commencement of the blood-flow, the mean pressure in the carotis was found to be 156 mm. hg. Nerve uninjured; there flowed out every 5 seconds

0 to 5	—10	—15	—20	—25 seconds.
1·0	1·0	1·3	0·9	0·9 c.cm.

The nerve was cut, 30 seconds afterwards the measurement of the outflow began, there flowed out every 5 seconds

30 to 35	-40	-45	-50	-55	-60	-65	-70	-75	-80	-85	-90	-95	-100 sec.
3·5	3·5	3·5	3·3	3·5	3·1	3·0	2·5	2·0	2·0	1·6	1·4	1·3	1·0 c.cm.

The flow of blood in the vein was now turned towards the heart, and the mean arterial pressure found to be 86 mm. hg. When, after the ending of this measurement, and after washing out the canula with carbonate of soda, the collection of the blood was renewed, there flowed out every 5 seconds

0 to 5	—10	—15	—20	—25	—30	—35 seconds.
1·8	1·8	1·8	1·7	1·4	1·0	1·6 c.cm.

The nerve was then again cut about a centimeter distant from the original point of section, and the estimation of the

flow continued without interruption. Every 5 seconds there flowed out

0 to 5	—10	—15	—20	—25	—30 seconds
1·6	1·7	1·4	1·4	1·3	1·2 c.cm.

Although the animal had suffered only a moderate loss of blood, yet but a few minutes after the last measurements he was dead.

In this case then, the second section caused no such increase of flow as occurred after the first; since, however, the animal that was the subject of the experiment behaved in many respects abnormally—the deep sinking of the arterial pressure and the sudden death after but a moderate loss of blood—and since I performed no other experiment with a double section of the nerve on animals not under the influence of some poison, I will leave it doubtful, whether mere section can constitute a stimulus to the dilatator nerves of sufficient strength to cause such a rapid increase of blood-stream as is generally observed.

As an explanation of the temporary increase of stream, it is possible to put forward the hypothesis, that it is due to the removal of tonicity owing to the section of vaso-constrictor nerve-fibres running in the trunk of the crural nerve. In order to comprehend the subsequent rapid diminution in the rate on this supposition, one must assume further, that in consequence of the stronger flow, there is developed a higher degree of elasticity in the vessel-wall, an assumption, the possibility of which can no longer be doubted since the experiments of Mosso. The following experiment with curare poisoning may serve to elucidate this alternative.

Dog slightly poisoned by injection of curare into the jugular vein; artificial respiration; nerve uninjured. There flowed out every 5 seconds

0 to 5	—10	—15	—20	—25 seconds.
2·0	1·6	1·6	1·6	1·3 c.cm.

After the canula had been washed out, the amount was measured for another five seconds before the nerve was cut, this showed 1·2 c.cm.; the nerve was now cut, the measurement of the outflow continuing all the while, it gave

0 to 5	—10	—15	—20	—25	—30	—35	—40 seconds.
1·7	2·3	3·3	2·9	2·2	1·2	1·2	1·0 c.cm.

The nerve was now stimulated by strong induction shocks, which caused no visible contraction in the muscles. The measurement of the blood-stream, which continued uninterruptedly, showed

0 to 5	—10	—15 seconds.
1·4	1·0	0·8 c.cm.

The stimulation was now interrupted for 10 seconds, during which there flowed out

0 to 5	—10 seconds.
0·7	1·3 c.cm.

The stimulation was again commenced, without any visible contraction of the muscle, the continuous measurement of outflow gave

0 to 5	—10	—15 seconds.
0·7	1·0	0·9 c.cm.

and after the end of the stimulation there flowed out

0 to 5	—10 seconds.
1·0	1·0 c.cm.

After the canula had been washed out with carbonate of soda, during which time the blood-stream was deviated towards the heart, the measurement again began. This produced in 5 seconds 1·0 c.cm. The nerve was thereupon cut a second time without interrupting the measurement of the flow:

0 to 5	—10	—15	—20 seconds.
1·0	0·9	1·0	0·9 c.cm.

After this the blood-flow, was turned for twelve minutes towards the heart, and then the flow every 5 seconds was found to be

0 to 5	—10	—15 seconds.
1·6	1·6	1·3 c.cm.

No marked change could be produced in this rate by means of a renewed stimulation of the nerve:

0 to 5	—10	—15 seconds.
1·3	1·7	1·6 c.cm.

and after the end of the stimulation

0 to 5	—10	—15	—20	—25 sec.
1·4	1·3	1·3	1·3	1·4 c.cm.

This experiment favours the hypothesis, that section of the nerve removes a previously existing tonicity. One can suppose that, analogous with the dilatator fibres running in the chorda tympani, those also which are present in the crural nerve of mammals are made inactive by curare. If this is so, then the only explanation for the increase of flow following upon section of the nerve, which is evident enough in the above experiment, even though less pronounced and more temporary than usual, is that a previous action of vaso-constrictor fibres is removed. This assumption is strengthened by the fact, that a stimulation of the peripheral end of the cut nerve by means of the interrupted current seemed somewhat to diminish the outflow from the vein, although a second section remained without effect upon the stream. Even if it is not proved by this single instance, that the increased flow following upon the section of the nerve is due to a removal of the normal tone, yet it teaches that there are contained in the crural nerve fibres which act as vaso-constrictors to the arteries of the quadriceps extensor group of muscles.

The presence of these vaso-motor nerves enables us to conceive how it is, that in numerous cases after the section of the nerve, and after the marked increase of flow that occurs during the first minute, has ceased, there is still a slighter quickening remaining. The fact that this latter does not always occur would seem to denote, that the vaso-constrictor fibres have not always been in a state of tonic stimulation before their section, in all the animals experimented upon. On the other hand, it is possible to explain this secondary quickening of the blood-flow without invoking the presence of vaso-constrictor fibres, for it may be due to the fact, that in every case, during the time when the stream was diverted towards the heart after the nerve had been cut, the peripheral end of the nerve was fixed in the electrodes, and this may have been a stimulus to the dilatator fibres sufficient to cause a slight temporary increase of flow, which would make itself manifest upon the rate-curve, only in those cases, where the measurement of the flow recommenced sufficiently quickly after the completion of this operation.

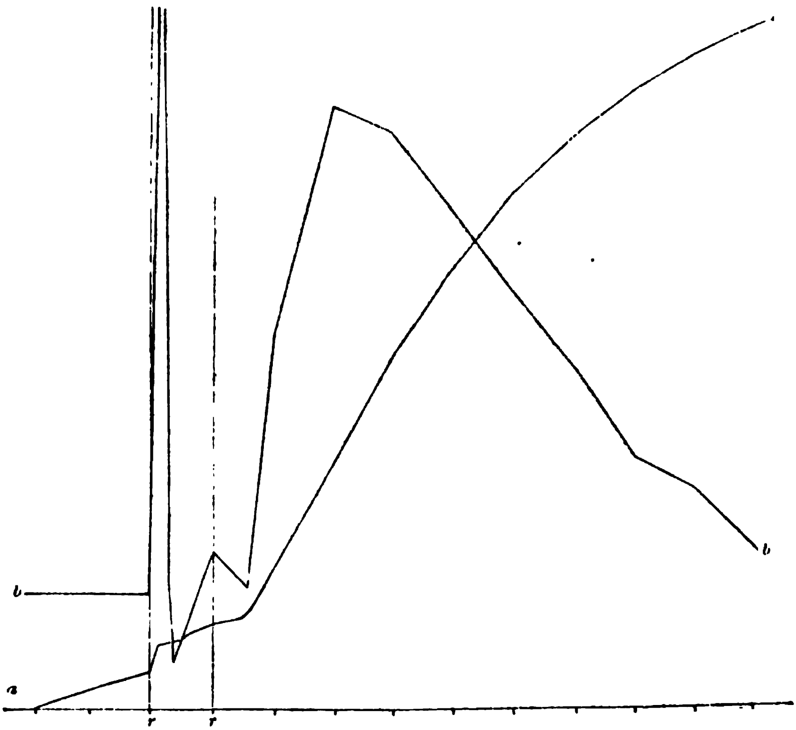
3. Changes in the blood-stream in consequence of stimulation of the nerve. Since that portion of the crural nerve

which can be placed on the electrodes contains nervous elements, some of which act upon the fibres, and others on the vessels of the muscles of the thigh, it is natural to think of resorting to curare. It is not possible however, in the case of dogs at all events, to effect the purpose in view by the use of this agent, since the curarized nerve loses the power to quicken the blood-stream simultaneously with the capacity to cause a contraction of the muscle. Although I abstained from using curarized animals for this reason, yet it might not be without point to make use of curare, provided that any suggestion gained by its means was otherwise confirmed. For instance, in the case of a dog, into which a moderate amount of this poison had been injected, it was found, after artificial respiration had been kept up until the animal began again to breathe of itself, that then the power of the crural nerve to induce contractions of the muscles returned, without however any sign of a simultaneous quickening of the blood-stream. The nerve therefore, when recovering from the effects of the poison, was brought into a condition, which might assist in solving the cause of the quickening of the stream, although it was not practicable for my immediate purpose. Seeing that many of the conditions of the experiment are continually varying at the same time, and that too in no fixed determinate manner, it is impossible to describe the phenomena, that occur in consequence of nerve stimulation, in terms of any one special variation of the experiment that may be chosen. For instance, there is a continual increase in the amount of blood lost, and at the same time a progressive exhaustion of the nerve; in addition to these, a phenomenon like ours, which depends on the relations between different kinds of nerve-fibres, must necessarily vary in different animals. Under these circumstances, it is of necessity preferable to describe the results themselves, rather than an analysis of them. In order to accomplish this as fully and thoroughly as possible, the total observations that were obtained from 14 dogs were accurately worked out, and out of the great number of separate experiments so obtained, those were chosen for publishing, which were remarkable for any special peculiarity. Nearly all the observations that are described are examples of many other similar ones.

Of these examples the second to the thirteenth are arranged in order of duration of stimulation, in some of them the effect of a greater and less loss of blood is compared together. The examples 14 and 15 refer to the action of tetanizing currents suddenly increased in strength.

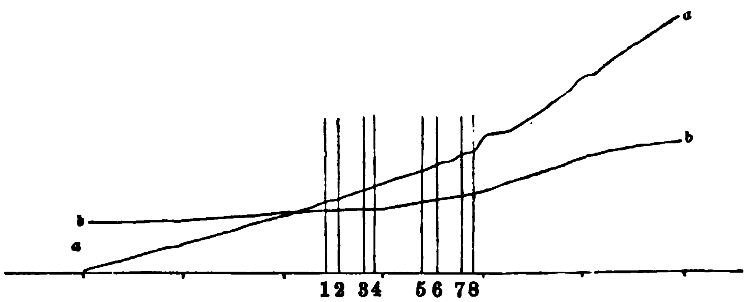
Although the changes in the rate of flow before, during, and after the stimulation of the nerve are clearly marked on the original curve, yet it is plain that they can be recognized with still greater clearness on the curve deduced from it; for this reason this deduced curve has been as a rule figured. An exception to this is made in the first example, where the deduced as well as the original curve is drawn, in order to make clear to the reader the origin of the former from the latter. For this purpose the lengths on the abscissa line representing divisions of time are made longer than in all later examples with the exception of the second, to the representation of which the original observation was also added.

Fig. 1.



The curve *aa* is photographed from the original and reduced half size. The curve *bb* is the deduced curve. Time intervals are marked on the common abscissa of the two curves. The distance between two points represents 5 seconds. The nerve was tetanized during the third unit of time *rr*. The body weight of the animal was 20·0 kilo. The crural nerve had been cut 4 minutes before the beginning of this observation, and the animal had already lost 154 c.cm. of blood = 0·77 per cent. of its body weight. Before the stimulation of the nerve there flowed out of the vein 2·3 c.cm. in every 5 seconds. During the tetanus of 5 seconds' duration, there flowed out from 0 to 0·75 sec. 4·0 c.cm.; from 0·75 to 1·75 sec. 0·1 c.cm., from 1·75 to 5 sec. 2·5 c.cm. After the cessation of the stimulation, there poured out in the 2 sec. immediately following 0·9 c.cm., and from there up to 5 sec. 5·5 c.cm. and then in successive 5 sec. 15·1 c.cm.—14·4 c.cm.—? c.cm.—10·1 c.cm.—8·3 c.cm.—5·9 c.cm.—5·1 c.cm.—3·5 c.cm. If one assumes that, during the 15th to the 20th second after the end of the stimulation, the velocity was the mean of that in the two neighbouring units of time, that therefore in this time 12·3 c.cm. had run out, then we should have an outflow of 87·6 c.cm. of blood during the 50 seconds that followed the commencement of the tetanus. The rate of flow before the stimulation would however, one may presume, have afforded only 23·0 c.cm. in the same time.

Fig. 2.

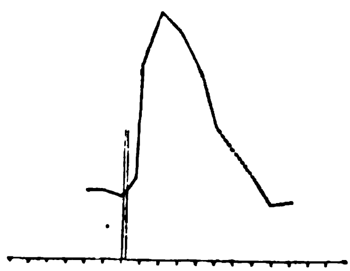


The curve *aa* is photographed from the original and reduced half size. The curve *bb* is the deduced curve.

Weight of animal 22·5 kilo. Before the stimulation 180 c.cm. of blood =0·8 p. c. of its body weight, had been expended. The pressure in the carotis was 156 mm. Hg. Starting with a considerable distance between the two coils, the secondary coil was gradually pushed closer, and stimulations, each lasting less than 0·1 sec., given at intervals up to the times denoted by the figures 1 to 7.

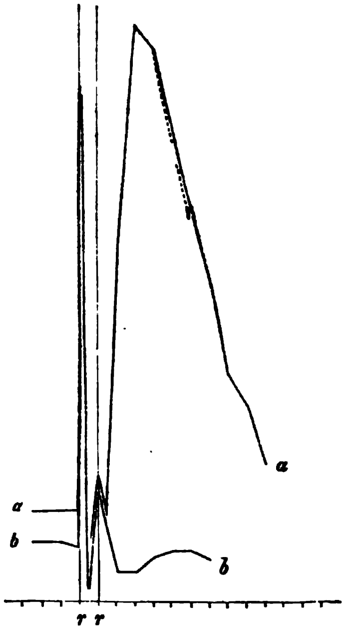
Before the first effective stimulation, there flowed out every five seconds 3·6 c.cm.; upon now closing the circuit three times in the course of 5 sec., the secondary coil being at that distance which produced the first signs of contractions, the amount of outflow rose in these five seconds to 4·3 c.cm. In the next five seconds the circuit was momentarily closed four times (1 to 4), after the secondary coil had been pushed a trifle nearer. In these five seconds there streamed out 4·6 c.cm. After the secondary coil had been moved yet further, four more momentary closures of the circuit (5 to 8) took place in the next five seconds, in consequence of which 6·1 c.cm. flowed out during this time. By means of the last three more powerful contractions, a marked after effect was now produced, for there flowed in the next two periods of five seconds 8·1 and 9·4 c.cm. respectively. Hereupon the measurement of the blood-flow was broken off.

Fig. 3.



Weight of the animal 12·8 kilo. Before the stimulation 81 c.cm. of blood = 0·6 p. c. of the body weight, had been expended. With the nerve at rest the amount of outflow for every 5 seconds fluctuated between 2·3 and 2·2 c.cm. Upon closing the circuit for 0·4 sec. (*rr*) there was seen to be a steady rise in the outflow, directly after the end of the stimulation, above that which existed before the closure, so that in the 5 seconds at the beginning of which the stimulation occurred 3·5 c.cm. flowed out, from there onwards, the amount of outflow increased in the next 5 seconds to 7·2 c.cm., and then sank in the following three 5-sec. intervals to 6·6—5·7—4·0. There flowed out therefore, in the 25 seconds at the beginning of which the stimulation occurred, 27·0 c.cm.; there would presumably have streamed out only 11·5 c.cm. in the same time, if there had been no stimulation.

Fig. 4.

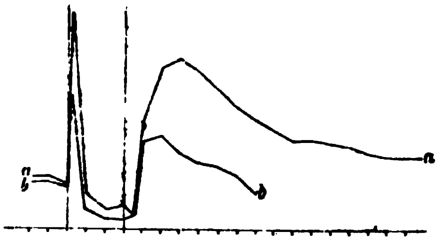


Of the two curves in this woodcut, the one between *aa* was obtained after at least 154 c.cm. of blood had been lost, the other between *bb* after a loss of at least 854 c.cm.

Weight of body 20·0 kilo.; nerve cut. Before the stimulation *rr* there flowed out every 5 seconds 2·3 c.cm. From the commencement of the tetanus there streamed out from 0 to 0·75 sec. 4 c.cm., from 0·75 to 1·75 sec. the flow ceased almost entirely (0·1 c.cm.), from 1·75 to 5 sec. 2·5 c.cm. In the 2 seconds following the end of the stimulation there flowed out 0·9, and from the 2nd to the 5th second 5·5 c.cm., from there onwards in succession for every 5 seconds 15·1—14·4—12·3—10·1—8·3—5·9—5·1—3·5 c.cm. The observation was here broken off. In 50 seconds therefore, at the beginning of which a tetanus of 5 seconds occurred, there streamed out 87·6 c.cm. of blood. It may be presumed that without any stimulation only 23 c.cm. would have flowed out in the same time.

The observation represented in curve *bb* took place after a loss of blood equal to 4·27 p. c. of the body weight. The amount of outflow for every 5 seconds before the stimulation *rr* fluctuated between 1·4 and 1·6 c.cm. At the beginning of the tetanus there spurted out from 0 to 0·7 seconds 3·5 c.cm., then the flow ceased entirely up to 2·1 sec., and from there up to the 5th second of the tetanus there flowed out 1·6 c.cm. In the 30 seconds which followed on the end of the stimulation, there poured out in successive 5 seconds 0·8, 0·8, 1·2, 1·3, 1·3, 1·0 c.cm. In the 35 seconds therefore, at the beginning of which a tetanus of 5 seconds occurred, there streamed out 11·4 c.cm.; without stimulation there would presumably have flowed out 10·2 c.cm.

Fig. 5.

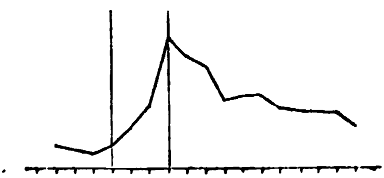


Dog of moderate size. The curve *aa* was obtained after but few c.cm. of blood had been lost, the curve *bb* after a loss of at least 250 c.cm.

Before the beginning of the stimulation *rr* there flowed out in every 5 seconds 1·2 c.cm. During the tetanus, which lasted 15 seconds, there streamed out in 0 to 1 sec. 1·1 c.cm., in 1 to 5 sec. 0·8 c.cm., in 5 to 10 sec. 0·5 c.cm., and in 10 to 15 sec. 0·6 c.cm. Upon the cessation of the stimulation there flowed out from 0 to 2·5 seconds 0·2 c.cm., and from 2·5 to 5 seconds 1·4 c.cm., and in the following 75 seconds in every 5 seconds successively 4·2, 4·5, 4·1, 3·7, 3·2, 2·9, 2·6, 2·4, 2·4, 2·3, 2·2, 2·0, 2·0, 1·9, 1·9. Therefore in 95 seconds, at the beginning of which a tetanus of 15 sec. occurred, there streamed out 46·8 c.cm. If the muscle had been at rest, only 25·2 c.cm. would have presumably flowed out.

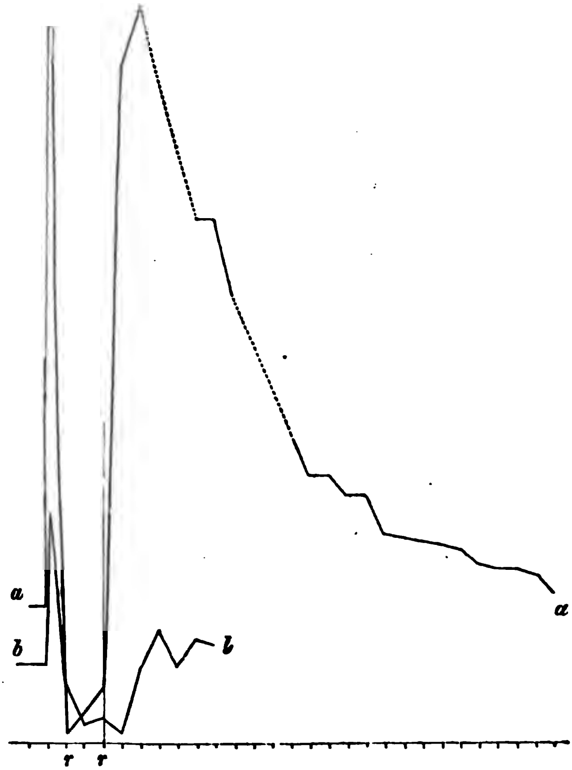
In the observation represented by the curve *bb*, the outflow before the stimulation fluctuated between 1·2 and 1·4 c.cm. for every 5 seconds. At the beginning of the tetanus there flowed out from 0 to 1 second 0·5 c.cm., in 1 to 5 seconds 0·4, in 5 to 15 seconds 0·5 c.cm. In the 35 seconds immediately after the end of the stimulation there poured out in successive 5 seconds 1·0, 2·5, 2·0, 1·8, 1·7, 1·4, 1·0 c.cm. Therefore in the 50 seconds, at the beginning of which a tetanus of 15 sec. took place, 12·7 c.cm. of blood streamed out; one may suppose that 13·0 c.cm. would have flowed out through the muscle at rest in the same time.

Fig. 6.



Dog of moderate size. This observation was made after a loss of blood exceeding 118 c.cm. Before the beginning of the stimulation *rr* the outflow in every 5 seconds fluctuated between 0·4 and 0·6 c.cm. During the tetanus of 15 seconds' duration there streamed out in successive 5 seconds 1·1, 1·7, 3·4 c.cm. In the 45 seconds after the end of the stimulation there flowed out in every successive 5 seconds 3·0, 2·7, 1·8, 1·9, 1·9, 1·6, 1·5, 1·4, 1·1 c.cm. Therefore in 60 seconds, at the commencement of which a tetanus of 15 seconds occurred, there poured out 23 c.cm. In the muscle at rest there would have flowed out, one may suppose, only 6·0 c.cm.

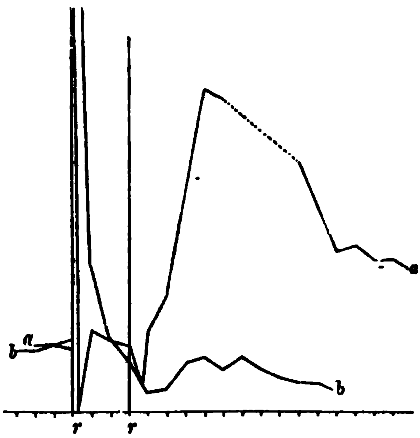
Fig. 7.



Weight of the animal 22·5 kilo. Before the beginning of the observation *aa* 251 c.cm. of blood had been expended; before *bb*, 772 c.cm.

Curve *aa*. Before the beginning of the stimulation the outflow in 5 seconds amounted to 3·6 c.cm., during the tetanus of 15 seconds there streamed out from 0 to 0·6 seconds 3·12 c.cm., from 0·6 to 5 seconds 0·3 c.cm., from 5 to 10 sec. 0·9 c.cm., from 10 to 15 sec. 1·6 c.cm. In the 70 seconds immediately following there poured in every 5 seconds successively 14·8, 19·2, 18·0, 15·0, 13·8, 13·8, 11·2, 10·5, 9·0, 8·1, 7·0, 6·5, 5·5 c.cm. Therefore in 85 seconds, at the commencement of which a tetanus of 15 seconds took place, there poured out 164·4 c.cm. In the muscle at rest, only 47·3 c.cm. would have presumably flowed out. In observation *bb* the amount of outflow before the stimulation was 2·1 c.cm in every 5 seconds. During the tetanus of 15 seconds there streamed out in 0 to 1 second 1·4 c.cm., in 1 to 5 sec. 1·2 c.cm., in 5 to 10 sec. 0·5 c.cm., in 10 to 15 sec. 0·7 c.cm. In the following 30 seconds there flowed out in successive 5 seconds 0·3, 2·0, 3·0, 2·1, 2·7, 2·6 c.cm. Therefore in 45 seconds, at the commencement of which a tetanus of 15 seconds occurred, there flowed out 16·4 c.cm.; in the muscle at rest one may suppose that 13·9 c.cm. would have flowed out.

Fig. 8

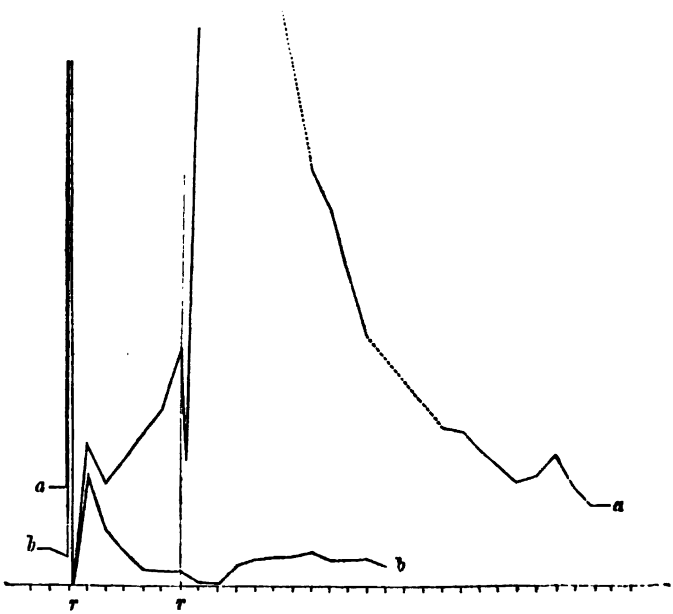


Body weight 86·5 kilo. Before the beginning of the observation *aa* 748 c.cm. of blood had been used; before *bb* 970 c.cm.

Curve *aa*. Before the beginning of the stimulation *rr* the mean of the outflow for every 5 seconds was 1·8 c.cm. During the tetanus of 15 seconds there flowed out in 0 to 0·6 seconds 4·7 c.cm., in 0·6 to 1·2 seconds 0 c.cm., in 1·2 to 5 seconds 1·8 c.cm., in 5 to 10 seconds 2·0 c.cm., and in 10 to 15 seconds 1·8 c.cm. After the end of the stimulation there streamed out in 0 to 3·5 seconds 0·5 c.cm., and in 3·5 to 5 sec. 0·7 c.cm. From there onwards there flowed out in every 5 seconds in succession, 8·1, 6·0, 8·6, 8·3 c.cm., and in the 70th to the 75th second the outflow still amounted to 3·8 c.cm.

Curve *bb*. Before the beginning of the stimulation the mean flow for every 5 seconds was 1·75 c.cm. During the tetanus of 15 seconds' duration there streamed out in 0 to 1·4 seconds 4·6 c.cm., in 1·4 to 5 sec. 3·0 c.cm., in 5 to 10 sec. 2·1 c.cm., and in 10 to 15 seconds 1·4 c.cm. After the end of the stimulation there flowed out in every 5 seconds successively 0·5, 0·7, 1·3, 1·4, 1·7, 1·4, 1·2, 0·9, 0·8 c.cm.

Fig. 9.

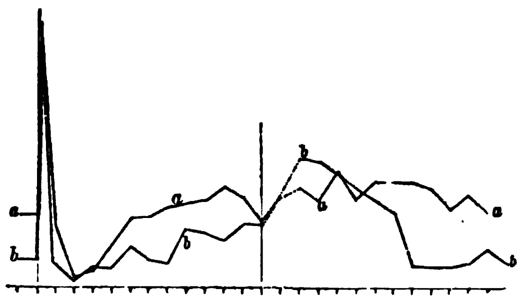


Body weight 20·0 kilo. Before the beginning of the observation *aa* 573 c.cm. of blood had been expended, before that represented by *bb* 900 c.cm.

Curve *aa*. Before the commencement of the stimulation there flowed out in every 5 seconds 2·6 c.cm. During the tetanus of 30 seconds there streamed out in 0 to 0·6 sec. 4·1 c.cm., in 0·6 to 1·6 sec. 0 c.cm., in 1·6 to 5 sec. 2·6 c.cm., in 5 to 10 sec. 2·7 c.cm., in 10 to 15 sec. 3·4 c.cm., in 15 to 20 sec. 4·0 c.cm., in 20 to 25 sec. 4·7 c.cm., and in 25 to 30 sec. 6·2 c.cm. From the end of the stimulation there flowed out in 0 to 1·5 seconds 1·0 c.cm., in 1·5 to 5 sec. 11·0 c.cm., and in 5 to 10 sec. 18·2 c.cm. Between the 10 and 15 seconds the measurement of the stream was interrupted, from there onwards followed in every 5 seconds successively 17·2, 16·1, 14·6, 11·1, 10·0, 8·2, 6·6, and so on.

Curve *bb*. Before the commencement of the stimulation there flowed out in every 5 seconds 0·85 c.cm.; during a tetanus of 30 seconds there streamed out from 0 to 0·8 sec. 3·2 c.cm., from 0·8 to 1·6 sec. 0 c.cm., from 1·6 to 5 sec. 2·0 c.cm., and then onwards in every 5 seconds in succession, 1·5, 0·9, 0·4, 0·4, 0·4 c.cm. After the end of the tetanus there flowed out during 40 seconds in every 5 seconds successively 0·1, 0·1, 0·5, 0·7, 0·8, 0·8, 0·9, 0·7 c.cm.

Fig. 10.

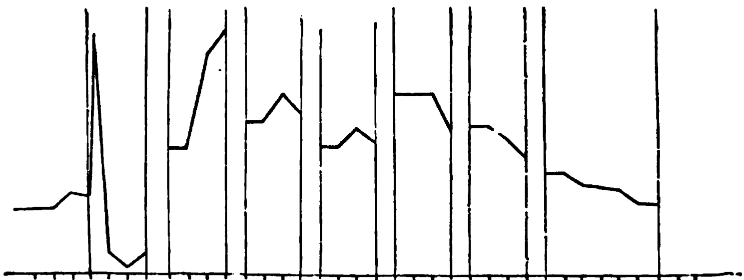


The curve *aaa* was attained after 45 c.cm. of blood had been used; before the curve *bbb* on the other hand, there was a loss of 260 c.cm.

Curve *aa*. Before the commencement of the stimulation there flowed out in every 5 sec. 1·9 c.cm. During the moderately strong tetanus of 1 minute duration there flowed out in 0 to 0·7 sec. 1·1 c.cm., in 0·7 to 5 sec. 1·4 c.cm. From there onwards there streamed out in successive 5 seconds, 0·3, 0·4, 1·1, 1·8, 1·8, 2·1, 2·2, 2·3, 2·6, 2·4, 1·8 c.cm. In 55 seconds after the end of the stimulation there flowed out in every 5 seconds successively 2·4, 2·6, 2·3, 3·1, 2·4, 2·8, 2·8, 2·8, 2·6, 2·1, 2·5 c.cm. Therefore during 115 seconds, at the beginning of which a tetanus of 60 seconds occurred, the whole outflow amounted to 49·0 c.cm. Presumably 34·5 c.cm. would have flowed out in the same time through the muscle at rest.

Curve *bb*. Before the beginning of the stimulation the outflow in 5 sec. was 0·7 c.cm., during a strong tetanus of one minute there streamed out in 0 to 0·7 sec. 1·1 c.cm., in 0·7 to 5 sec. 0·5 c.cm., and from there onwards in successive 5 seconds 0·2, 0·5, 0·5, 1·1, 0·7, 0·6, 1·5, 1·4, 1·2, 1·7, 1·7 c.cm. In 60 seconds after the end of the stimulation there flowed out in every 5 seconds successively 2·6, 3·4, 3·3, 3·0, 2·6, 2·3, 2·0, 0·6, 0·6, 0·6, 0·7, 1·1, 0·7 c.cm. Therefore in the space of two minutes, at the commencement of which a tetanus of one minute took place, there flowed out 30·4 c.cm. Presumably in the same time 16·8 c.cm. would have streamed out through the muscle at rest.

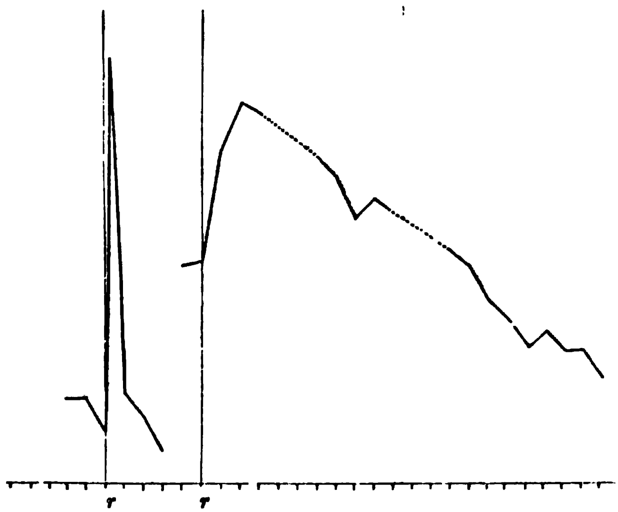
Fig. 11.



Body weight of animal 9·4 kilo. Before the beginning of the experiment represented by the curve, a loss of 104·0 c.cm. of blood had taken place. The amount of blood which flowed out in every 5 seconds before the tetanus fluctuated between 2·1 and 1·8 c.cm. The tetanus was to last at least 5 minutes; in order to keep it at a constant maximum strength during this time, the position of the leg was carefully watched, and every time it showed the least sign of relaxation, the secondary coil was moved nearer to the primary, until the limb had again returned to its old position. Since it was impossible, partly in consequence of clotting, partly on account of the large amount that would have been expended, to allow the blood to flow out during the whole course of the tetanus, the measurements took place only at intervals, in such a manner that at the commencement of every fresh minute the blood streamed into the measure glass for 15 seconds, while during the rest of the time it could flow on to the heart. In the curve the pauses P between the successive measurements are included between two upright lines.

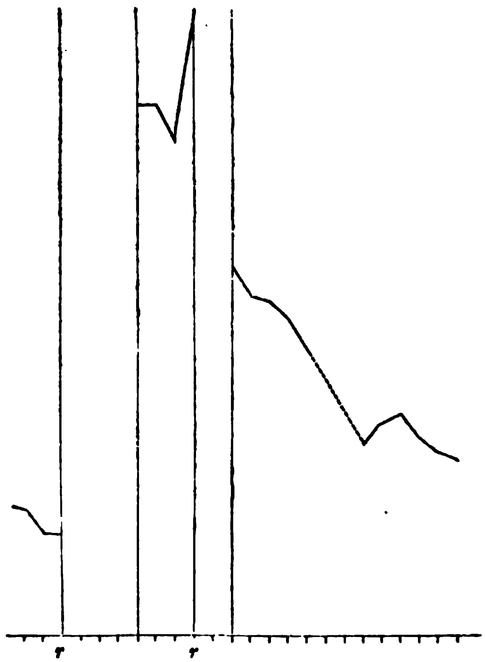
In the first 15 sec. of the tetanus there flowed out from 0 to 0·7 sec. 1·0 c.cm., from 0·7 to 5 sec. 0·4 c.cm., and then in successive 5 seconds 0·3 and 0·4 c.cm. In 60 to 75 sec. there flowed out in every 5 seconds in succession 3·3, 5·8, 6·7 c.cm., in 120 to 135 sec. in successive 5 seconds 4·0, 4·8, 4·3 c.cm., in 180 to 195 sec. 3·4, 3·9, 3·5 c.cm., in 240 to 255 sec. 4·8, 4·8, 3·9 c.cm., in 300 to 315 seconds 3·9, 3·6, 3·2 c.cm. Twenty seconds after the ending of the tetanus the flow was again conducted into the measure glass, and during 30 seconds there flowed out in every 5 seconds successively 1·8, 1·5, 1·4, 1·3, 1·0, 1·0 c.cm.

Fig. 12.



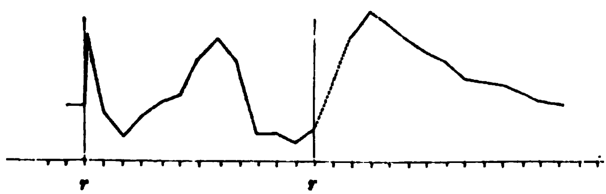
Body weight 22·5 kilo. Before the beginning of this experiment a loss of blood amounting to 612·0 c.cm. had taken place. The outflow before the stimulation of the nerve fluctuated between 2·3 and 1·4 c.cm. in every 5 seconds. During the tetanus, which was kept constant by moving the secondary coil nearer, the blood was allowed to run into the measure glass only during the first 15 and the last 10 seconds, for the rest of the time it flowed to the heart. There streamed out from 0 to 0·8 sec. 1·8 c.cm., from 0·8 to 5 sec. 2·1 c.cm., from 5 to 10 sec. 1·8 c.cm., and from 10 to 15 sec. 0·9 c.cm., and then from 290 to 295 sec. 5·9 c.cm., from 295 to 300 sec. 6·0 c.cm. Immediately after the stimulation there flowed out in successive 5 seconds 8·9, 10·1, 9·9, 9·5, 9·0, 8·7, 8·2, 7·2, 7·7, 7·3, 6·9, 6·5, 6·3, 5·8, 4·9, 4·4, 3·8, 4·2, 3·6, 3·6 c.cm.

Fig. 13.



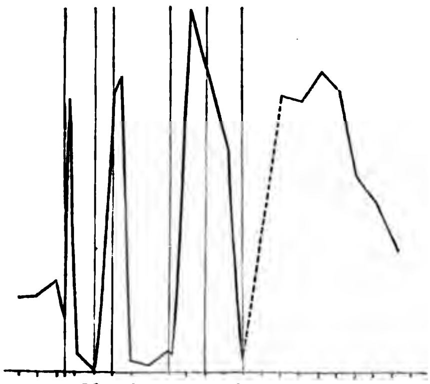
Body weight 36·5 kilo. Before the beginning of the tetanus there flowed out 2·7 c.cm. in every 5 seconds. Up to the beginning of the tetanus, which was kept as constant as possible for 19 minutes by continually increasing the strength of the induction current, the animal had lost 580 c.cm. of blood. The blood-stream was conducted into the measure glass only during the last 15 seconds of the tetanus, during which time there flowed out every 5 seconds in succession 14·2, 13·3, 16·6 c.cm. After the end of the stimulation the measurement was interrupted for 10 seconds, then however it gave for successive 5 seconds 9·6, 9·1, 9·0, 8·4, 7·7, 6·8, 6·0, 5·2, 5·7, 6·0, 5·3, 4·9, 4·8 c.cm.

Fig. 14.



Up to the beginning of the observation the animal, which was of moderate size, had lost at least 200·0 c.cm. of blood. Before the beginning of the stimulation there flowed out in every 5 seconds 1·7 c.cm. The tetanus lasted a minute with however inconstant strength; at first strong, it gradually subsided and then in about 40 seconds was again suddenly made strong by moving the secondary coil nearer. From 0 to 0·9 sec. there poured out 0·7 c.cm., from 0·9 to 5 sec. 1·1 c.cm., from there on there streamed out in successive 5 seconds 0·8, 1·3, 1·7, 1·8, 2·8, 3·3, 2·7, 0·8, 0·8, 0·5, 0·9 c.cm. Five seconds after the conclusion of the stimulation the measurement of the outflow recommenced; this showed in successive 5 seconds 2·1, 4·0, 3·7, 3·2, 2·9, 2·6, 2·2, 2·1, 2·0 c.cm.

Fig. 15.



Body weight 12·8 c.cm. Before the beginning of the experiment the animal had lost about 100·0 c.cm. of blood. In this observation 3 tetani followed close on each other with short intervals between. The length of time that the nerve was not under stimulation was determined by the strength of the outflow in the so-called after-effect. As soon as this was developed in a high degree, then a new stimulation was thrown in. The first tetanus *R*1 lasted 8 seconds, during it there flowed out from 0 to 0·8 sec. 0·9 c.cm., from 0·8 to 3 sec. 0·3 c.cm., from 3 to 8 sec. 0·1 c.cm. In the 5 seconds following the stimulation, the amount of the outflow increased to 7·8 c.cm. Immediately a tetanus *R*2 of 15 seconds duration was thrown in. During this there flowed out in 0 to 1·6 sec. 2·3 c.cm., in 1·6 to 5 sec. 0·3 c.cm., in 5 to 10 sec. 0·3 c.cm., in 10 to 15 sec. 0·7 c.cm. The stimulation being now interrupted for 5·5 seconds, the amount of outflow in every 5 seconds increased to 9·6 c.cm. The new stimulation of 15 seconds which now commenced, proved at first not to be strong enough to cause a tetanus, there streamed out during this insufficient stimulation in 5 sec. 7·3 c.cm. The strength of the induction current was therefore increased and during the tetanus *R*3 so caused, there poured out in the first 5 sec. 4·8 c.cm. and in 5 to 10 sec. 0·5 c.cm. The next 5 seconds after the ending of this tetanus were used for the washing out of the canula, and after that there flowed out in successive 5 seconds 7·3, 7·2, 7·9, 7·4, 5·2, 4·6 c.cm.

With reference to the phenomena exhibited in the foregoing experiments, I will now draw attention to the position and number of the essential points, which characterize the rate-curve from the beginning of the stimulation to the return of the normal outflow. The chief variations in the rise and sinking of the rate of flow, that are noticeable in these curves are, as a rule, the following: with the commencement of the tetanus there appears a spurt-like quickening of the stream, followed on further contraction by an almost complete cessation of flow, which then again steadily and gradually increases in volume; at the end of the tetanus, the rate of flow sinks a second time for a moment and then rises again in the course of some seconds to a new maximum, from which it falls gradually and much more slowly than it arose to near the value it possessed before the stimulation. Although this sixfold change of rate occurs often enough for one to consider the curve deduced from it as a typical one (see among others the curves 1, 4, 5*a*, 8), yet it is by no means always manifested; on the contrary, one or other of the characteristics of the curve that I have just mentioned is often wanting. Thus the sudden outspurt of the blood occurring at the onset of the tetanus may fail (see the woodcuts 3 and 6), a circumstance that naturally occurs but seldom. Further, the increase of rate during the tetanus may be wanting, or only manifest itself but slightly (see Fig. 5 and curve *b* in Fig. 7). This characteristic of the curve fails most commonly, though by no means always, when the tetanus does not last so long as fifteen seconds; if it lasts longer, then on the contrary even during its continuance the outflow may attain a volume many times as great as that of the normal stream. The temporary diminution of rate that occurs when the muscular fibres pass from a state of contraction to one of relaxation may also be absent (see Fig. 7, curve *a*, and Fig. 9, curve *b*). Also the position of maximum velocity is variable. For although, apart from the outspurt of blood at the commencement of the tetanus, the flow, as a rule, first attains its greatest height after the cessation of the nerve-stimulation, yet it is possible for this to be manifested even during the tetanus (see Fig. 10).

The solitary variation of flow, which was never missing

in the case of animals not under the influence of any poison, was the strong and gradual increase which follows upon a short tetanus, and accompanies a long one even during a part of its duration. Should however the observation before mentioned be confirmed, viz. that a tetanized nerve which is commencing to recover from curare poisoning is in a position to effect a contraction of the muscle and yet not quicken the outflow of blood, there would clearly be no strong connection between the shortening of the muscle fibres and the swelling of the blood-flow.

However that may be, it may be considered as proved, that a part of the usual peculiarities of the flow may be wanting, without one being able to assign as a reason for this, either the nature of the nerve-stimulation, or the contraction of the muscular fibres, or the rest of the evident causes of change of rate. From this it follows, that by the stimulation of nerves acting on the muscular fibres only, all the conditions are not fulfilled, which are essential to the course of the curve of variable rate. Every phase of the latter then demands the presence of special causes. If one considers what these may be, one finds without difficulty a number of conditions, which at least suffice to explain every change of rate.

Since the shape of the muscle changes with the contraction, so too, as is evident, will the tension between its separate fibres. In consequence, different resistances will be opposed to the blood-stream, according as it flows through the contracted or relaxed muscle, and new forces will be added to it at the moment of transition from the one form to the other. It is natural therefore to attribute the sudden outspurt of blood, which accompanies the onset of the contraction, to a sudden diminution of the calibre of certain portions of the muscular vascular tract. The second diminution of the rate, which usually follows immediately on the cessation of the muscle contraction, one would, corresponding to this, have to attribute to the refilling on the termination of the contraction of those spaces, which were emptied at the commencement of the same. Which are the portions of the vascular tract, that are narrowed by the contraction of the muscle, may be left undecided, until we have obtained some more definite evidence. In the mean

while, one is compelled to consider it probable, that it is not the lumen of the capillaries which is pressed together by the shortening of the muscle fibres. It would at all events be difficult to make the assumption that the capillaries are narrowed, agree with the fact, that during a long continued steadily strong tetanus the rate of flow can increase to a height far surpassing that with which the blood flows through the muscle at rest.

The nerve-trunk that is stimulated contains, as we have already been obliged to conclude from the results of its section, nerves acting on the vessels, and probably nerve-fibres of two kinds, constricting and relaxing fibres. The acceptance of fibres that dilate the vessels in the nerves which supply the muscles of the dog, has still further grown in probability, as I have since succeeded in discovering nerves of this nature in the case of the mylo-hyoid muscle of the frog[1]. If one however assumes, that by the tetanizing of the crural nerve the two kinds of vaso-motor nerves are stimulated at the same time, then not only the usual phenomena but also all other deviations from them admit of explanation. A series of experiments, which v. Frey has performed with Prof. Ludwig in the Laboratory at Leipzig, has shown that, in the case of the simultaneous stimulation of the vaso-constrictor and vaso-dilatator nerves of an organ, the action of the first of the two gets the mastery, while on the contrary, after cutting off the two nerves from the induction current, the action of the dilatator fibres becomes manifest. Applying this rule to my experiments, all those cases would come under it where the rate of outflow was less than the normal during the stimulation, but rose above the normal after the cessation of the same. If one in addition takes into consideration the small power of endurance in the vaso-constrictor nerves of the muscle, as observed by Hafiz, then it is clear, why as a rule in the case of stimulations lasting longer than 15 seconds, a decided rise in the rate occurs even during the tetanus. Should however observations occur, to the explanation of which the theories hitherto suggested are not sufficient, then one would be driven to think of changes in the chemical composition of the vessel wall caused by the well known decompo-

[1] *Centralblatt für d. med. Wissenschaften*, 1876, p. 557.

sition products, which arise from the contraction of the muscle. I however have never met with any observation, which made such an explanation necessary, since the time when I succeeded in preventing the stagnation of the blood in the muscle; on the other hand, I have met with facts which speak against this theory. For, if any one of the manifold variations of the blood-stream through the stimulated muscle ought to be ascribed to a chemical change in the walls of the vessels, it surely must be that increase of flow, which takes place during the first seconds after the termination of a short or during the later seconds of a longer lasting tetanus. For at this time the products of decomposition that are produced within the muscle must be the most plentiful. If then the relaxation of the vessel wall is to be attributed to a change in chemical composition, it ought not to be removed either by the entrance of a new stimulation or by the strengthening of a previous stimulation. This however does happen, as the observations show (see Figs. 14 and 15). In observation 14 the strength of the stimulation was suddenly increased, after it had already kept the muscle steadily in a state of tetanus for 35 seconds, and in consequence had caused a considerable quickening of the blood-flow; immediately the rate of flow sank again down to a value, which was even below that which existed shortly after the commencement of the tetanus. In observation 15 a second stimulation was given, at times when the increase of stream had attained its maximum after a tetanus lasting 10 and 15 seconds respectively. Immediately on the entrance of the new stimulation,, the strong jet of blood was converted into a flow by drops.

The relations of the magnitudes of the fluctuations in the rate to the variations in the stimulation is much less clearly brought out in the experiments, than the time relations. The principal obstacle to the more accurate estimation of this relation consists in the fact, that any two observations arranged for different durations and strengths of stimulation were of necessity carried out after a loss of blood unequal in amount in the two cases. Experiment shows the effect of this latter to be, that the action of a given stimulation diminishes with the diminishing amount of blood contained in the body, in a proportion which cannot be more nearly defined. This difficulty,

which cannot be avoided on account of the method of observation chosen, does not however cause so great an effect as to obscure the direction in which the variations of the stimulation in duration and strength differ from each other, with respect to their effect on the blood-stream. For, since the loss of blood weakens the result of a stimulation on the stream, one can conclude with certainty, that that stimulation had a more powerful action, which, although it came into operation after a greater loss of blood, yet increased the velocity of flow to a still greater degree than another, which occurred when the animal possessed a more plentiful supply of blood. As an example of this, one of the successful series of experiments will suffice, which was performed on a dog whose weight before the beginning of the experiment was 20·0 kilo. The meaning of the numbers is apparent from the letter press.

	Length and strength of stimulation.	Outflow before stimulation in 5 sec.	Maximum of the flow after stimulation in 5 sec.	Duration of the increase of flow beyond the normal.	Amount of blood lost before the commencement of the stimulation.
1.	5 seconds separate contractions.	2·4 c.cm.	5·0 c.cm.	25 sec.	114 c.cm.
2.	5 seconds strong tetanus.	2·3 "	15·1 "	longer than 45 sec.	154 "
3.	10 seconds strong tetanus.	2·1 "	12·9 "	longer than 50 sec.	264 "
4.	15 seconds strong tetanus.	1·3 "	19·0 "	longer than 115 sec.	346 "
5.	30 seconds strong tetanus.	?	11·2 "	longer than 115 sec.	566 "

These figures clearly show that a tetanus has more influence than a series of separate stimulations, not only on the duration, but also on the maximum value of the increased flow, and that a tetanus of 15 or 30 seconds is more effective in both these directions, than one of five seconds' duration. One cannot speak more definitely.

The results of stimulation, under varying blood contents of the animal, help to make clear the influences which condition the increase of flow, especially as it is possible to effect as great a bleeding of the animal from this vein by means of a series

of stimulations following one another, as by the opening of the two carotids. Although the experiments were by no means devised, in order to carry the bleeding from the vein as far as possible, yet it has happened during them, that the animal has lost as much as 4·5 per cent. of its body weight in blood; and the loss per cent. could have been raised yet higher, if the experiment had not been broken off for other reasons.

It has already been conjectured, that the outspurt of blood, which accompanies the onset of a tetanus, is dependent upon the pressing out of certain of the contents of the vessels of the muscle in consequence of the change of form in the muscle. It follows from this assumption, that the amount of blood thrown out by the commencing tetanus must be to a great extent independent of the quantity of blood in the animal. The amount of blood contained in the more yielding vascular tracts, especially therefore in the veins, is as we know from experience conditioned in a much higher degree by the resistance to the outflow, than by the strength of the inflow. Since then, according to the observations already communicated, the first remains at all times nearly unaltered, it follows that, as far as the lumen of the veins is influenced by the onset of the tetanus, the amount of blood pressed out at the commencement of the stimulation must also remain unchanged. The following table confirms this. The plan, by which this table was formed, will be easily understood by the help of the following remarks. The series of Roman numbers, in front of which "Order of the tetani" stands, are numbers representing the order in which the tetanizing shocks followed each other during the course of the experiment. The series with the word "Outspurt" in front, gives the volume of blood in c.cm. which was thrown out in a fraction of the first second of the tetanus. The series after the words "Flow during rest" indicates the volume of blood in c.cm., which streamed out of the vein during five seconds before the commencement of the stimulation. The numbers after the words "Loss of blood" measure in c.cm. the volume of blood, which the animal had lost up to the commencement of that particular stimulation denoted by the Roman number standing above. In the table, only those observations are recorded, in which a pause of some minutes occurred between two consecu-

tive stimulations, during which time the stream out of the muscle flowed towards the heart.

A.

Order of the tetani.	I.	III.	IV.	V.	VI.
Outspurt.	2·73	4·68	4·29	3·77	4·55
Flow during rest.	?	1·69	?	1·61	1·75
Loss of blood.	487	740	870	930	970

B.

Order of the tetani.	I.	II.	III.	V.
Outspurt.	0·75	0·95	1·30	2·28
Flow during rest.	2·48	1·82	0·95	0·80
Loss of blood.	55	104	184	302

C.

Order of the tetani.	III.	IV.	V.	VI.	VII.	VIII.
Outspurt.	4·02	3·90	4·03	4·10	4·16	3·77
Flow during rest.	2·34	2·14	1·20	?	1·88	?
Loss of blood.	154	246	345	566	774	833

Order of the tetani.	IX.	X.	XI.	XII.	XIII.
Outspurt.	3·51	3·51	3·15	3·23	3·50
Flow during rest.	1·50	1·23	1·08	?	1·13
Loss of blood.	849	863	876	891	909

D.

Order of the tetani.	I.	III.	IV.	V.	VI.
Outspurt.	3·12	2·60	1·82	1·43	1·69
Flow during rest.	3·64	2·08	1·88	2·08	?
Loss of blood.	255	606	616	772	788

E.

Order of the tetani.	I.	II.	III.	IV.	VI.	VII.	VIII.
Outspurt.	1·13	1·05	0·88	0·43	0·70	0·52	1·05
Flow during rest.	1·23	?	1·05	?	?	1·23	0·70

As the results show, the amount of blood thrown out from the commencement of the tetanus to the stoppage of the flow is quite independent of the previous loss. Sometimes the volume of the same remains nearly unaltered in successive stimulations, in spite of a rapid increase in the loss of blood, sometimes it even rises again in the period near that, at which death from bleeding would occur. Therefore the fluctuations in its magnitude must depend on other conditions than the amount of blood in the animal. Since however the deviations in value are but small throughout any one experiment, these conditions may be found in small changes in the capacity of

the veins, occurring before the beginning of the different stimulations, owing to the unanæsthetized animal not always keeping the limb in the same position.

From the numbers which stand in the third row of the above table, after the words "Flow during rest," it appears that the rate of blood-flow from the vein of the muscle at rest diminishes on the whole with the increasing loss of blood, though by no means in proportion to this increase.

The rate at which the blood flows after the tetanus, on the other hand, depends most markedly on the quantity of blood in the animal; the following table shows this. The numbers in it are arranged similarly to the last; it is only necessary to add to the explanations given there, that the Arabic numbers in the first row of every experiment, which are printed close to the Roman ones, denote the time of the duration of each tetanus. As a measure of the magnitude of the outflow during the period after the tetanus, I have chosen the maximum value that was observed in any five seconds of this period. I was obliged to limit myself to this method of estimation, because, in by far the most of my observations, it was impossible to continue the bleeding until the more rapid stream produced by the stimulation had again returned to its normal value; I also considered the estimate I have given sufficient for the above purpose, because it appears to be the rule, that the stream reaches the normal so much the quicker the smaller the maximum rate attained has been. Figs. 4, 5, 7 serve as examples of this.

A. Body weight 36·5 kilo.

Order and duration of the tetani.	I. (15 sec.)	II. (19 min.)	III. (15 sec.)	IV. (15 sec.)	V. (30 sec.)	VI. (15 sec.)
Maximum of the after-flow.	7·15	16·6	8·58	4·94	2·86	1·43
Flow during rest.	?	?	1·69	?	1·61	1·75
Loss of blood.	487	580	740	870	930	970

B. Body weight 9·4 kilo.

Order and duration of the tetani.	I. (6 sec.)	III. (8 sec.)	IV. (5 min.)	V. (15 sec.)
Maximum of the after-flow.	7·35	6·03	1·93	6·30
Flow during rest.	2·48	0·95	0·45	0·80
Loss of blood.	55	184	250	302
Pressure in carotis.	156 mm.	125 mm.	74 mm.	51 mm. (at end of after-flow.)

C. Body weight 20·0 kilo.

Order and duration of the tetani.	III. (5 sec.)	IV. (10 sec.)	V. (15 sec.)	VI. (30 sec.)	VII. (15 sec.)	VIII. (10 sec.)
Maximum of the after-flow.	15·08	12·86	18·98	18·20	6·50	1·56
Flow during rest.	2·34	2·14	1·20	?	1·88	?
Loss of blood.	154	246	345	566	774	833

Order and duration of the tetani.	IX. (5 sec.)	X. (10 sec.)	XI. (15 sec.)	XII. (30 sec.)	XIII. (30 sec.)
Maximum of the after-flow.	1·30	1·17	1·05	0·88	1·44
Flow during rest.	1·50	1·23	1·08	?	1·13
Loss of blood.	849	863	876	891	909

D. Body weight 22·5 kilo.

Order and duration of the tetani.	I. (15 sec.)	II. (5 min.)	IV. (5 min.)	V. (15 sec.)	VI. (5 min.)
Maximum of the after-flow.	19·24	13·52	10·14	2·99	4·16
Flow during rest.	3·64	3·12	1·88	2·08	?
Loss of blood.	255	480	616	772	788
Pressure in carotis			88 mm.	28 mm.	

E. Body weight ?

Order and duration of the tetani.	I. (15 s.)	II. (1 m.)	III. (15 s.)	V. (15 s.)	VI. (1 m.)	VII. (15 s.)	VIII. (1 m.)
Maximum of the after-flow.	4·45	2·63	3·50	2·8	4·0	2·45	3·41
Flow during rest.	1·23	?	1·05	0·92	?	1·23	0·70

Since the tension in the arteries sinks with the increase of the loss of blood, one would expect under all circumstances, that the quickening of the blood-stream which occurs after the end of the nerve stimulation would diminish in a corresponding degree. There would have been no need for the above table in order simply to testify to this fact. It was impossible however to predict beforehand the law after which the outflow would diminish with the increasing loss of blood, and about this we obtain some insight from the above series of figures. Thus, for example in experiment A, there are 4 stimulations of 15 seconds duration occurring after different amounts of blood had been expended. When the loss of blood, which before the first stimulation had amounted to 487 c.cm., had increased to 740, i. e. by the considerable amount of 253 c.cm., the maximum rate had not as yet diminished, for the maximum volume of outflow in 5 seconds after the first tetanus amounted to 7·2, after the second to 8·6 c.cm. Although now only 130 c.cm. of blood flowed out between the second and third tetanus, yet the volume of the flow in 5

seconds during the time of maximum rate fell to 4·9, i.e. to 0·57 times the former value. And though between the third and fourth tetanus a further loss of only 100 c.cm. was recorded, yet the volume that flowed out during the time of maximum rate diminished to 1·4 c.cm., i.e. to 0·16 times the amount measured after the second, and 0·28 times that after the third tetanus. In this animal then, no fall in the maximum rate could be noticed in consequence of the rising loss of blood, as long as the amount lost did not exceed 2 per cent. of its body weight. As soon however as the amount arose above this limit, then proportionately small losses of blood diminished the maximum rate, which occurs after the end of the tetanus, to such a marked extent, that it decreased much quicker than the blood contents of the animal. The observations obtained from the 4 other animals correspond with this. Since however neither the amounts of blood lost, nor the times of tetanizing were arranged from the point of view just expressed, they are not suitable for the deduction of a law; though they appear good enough to draw attention to the question suggested, the answering of which would be of importance, as well for the nutrition of the muscle in individuals with a poor supply of blood, as for the regulation of the resistances to the blood-stream in the case of varying amounts of blood.

The figures make us acquainted with another peculiarity, which happens to the blood-flow through the repeatedly tetanized muscle of an animal that is deficient in blood supply. In the animals A. (tet. VI.) and B. (tet. IX. to XI.) the maximum reached by the outflow during the time immediately following the tetanus is very nearly equal to or even smaller than that occurring before the beginning of the stimulation. If one were to conclude from this, that there is an essential difference between the changes produced in the flow through the muscle of an animal that is deficient in blood, by the stimulation of its nerve, and those in an animal that is rich in blood, then the curves which show the whole course of the variations in rate will teach us the contrary, see Figs. 8 and 9. In accordance with these diagrams, the chief difference between the flow through the muscle of an animal rich in blood and another

poor in blood is seen to consist essentially in this, that those portions of the curve, in which the stream sinks below the normal strength, last longer under the latter circumstances than the former, and that the quickening of the stream after the end of the tetanus reaches a much smaller height in animals that are deficient in blood. Since the phenomena observed were noticed after the nerve had been repeatedly stimulated, and at the same time the arterial pressure much lowered, it is impossible with certainty to make either the deficiency of blood alone or the exhaustion of vaso-dilatator fibres answerable for its occurrence, though probability would rather point to the first explanation.

After the facts communicated in this paper, it is no longer possible for any one to doubt, that the rate of the blood-flow through the muscle of an uninjured animal is subject to variations similar to those observed under the conditions, which were realized in Sadler's and my experiments. If then one is to make use of the facts of these experiments to explain what occurs in the natural condition, one must above all make sure, how far the conditions in the two cases correspond. If the spurt-like quickening of the stream, which occurs at the onset of the contraction of the muscles, depends truly only on the change of form in the muscle, then it will take place on every kind of stimulation whether artificial, reflex or voluntary. The case may be different however with the weakening of the stream during the first seconds of the tetanus, and with the flooding which takes place regularly after the termination of a tetanus, or during it in the case of a long tetanus. If these two peculiarities of the flow owe their origin to the stimulation of nerves which differ both from each other, and speaking in a narrow sense, from the muscle nerves, then it is of course questionable, whether stimulation of them too comes into play in the case of voluntary and reflex movements.

I had no opportunity of observing, whether the rate of stream diminishes a short time after the commencement of a tetanus caused either by reflex or voluntary action; I would not have any one conclude from this remark, that this does not occur, for I never set myself to find out how the stream

behaves during a contraction caused by natural stimuli. However, by mere chance observations, one cannot overlook the fact, that the blood-stream is quickened strongly and in a more or less lasting manner every time that the animal, before the section of the nerve, moves of its own accord those muscles, from which the open vein proceeds. It appears then that in this respect also there is an agreement between the phenomena of secretion in the salivary glands and the contraction of a muscle, in that both are accompanied by a rapid blood-flow, which must in many ways assist the mechanism by which these actions are produced.

Since, as I have said, I have conducted no methodical series of observations on muscles contracting either by voluntary or reflex action, I am not in a position to throw any light on the nature of the quickening during a tetanus produced naturally or reflexly. Inquiry into the same may be left for later researches.

I have thought it best to leave this paper as it was originally written, rather than to modify it in accordance with my later experiments on the vessels of the mylo-hyoid muscle of the frog. The description of these experiments, and the alterations that they have caused in some of the views expressed here, will I hope form the subject of a future paper.

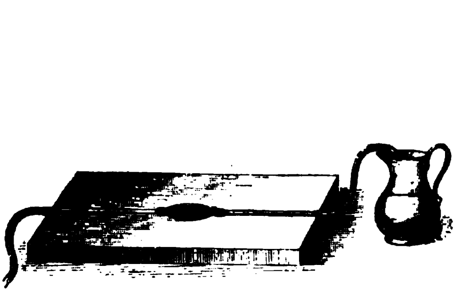
A CIRCULATION STAGE, A LIVE-DEVELOPMENT SLIDE, AND AN IMPROVED DRAWING REFLECTOR. By H. A. Reeves, *Assistant Surgeon and Teacher of Practical Surgery at the London Hospital.*

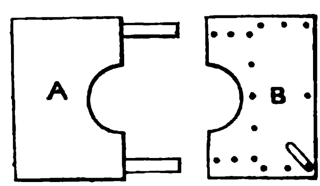
Although several forms of apparatus have been devised for the study of the circulation, whether normal or in inflammation, in fish and amphibia, only one means at all satisfactory has been hitherto used in the examination of the circulation in warm-blooded animals, and that is the Sanderson-Stricker apparatus for the omentum of the guinea-pig, and, perhaps, the rabbit. This, though undoubtedly a great advance, is somewhat complicated, and cannot be applied to the examination of other parts, as, for instance, the third eyelid or nictating membrane.

To meet this difficulty I have devised a stage, to be fitted to ordinary microscopes, which can be used in the *upright position* of the instrument, and which I think will meet with the approval of practical histologists, as it can be used for birds, rabbits and small dogs. The diagram, Fig. 1, will show that it consists of two parts, *A* and *B*, which may be separated by simply drawing them apart, and which are kept fixed by arms *dd* sliding into sockets in *B*, which has perforations for *grooved* pins on which the part to be examined is fixed. This figure represents the stage closed as for ordinary use, but when the circulation is to be studied *A* is withdrawn, and the anæsthetized animal is brought to the left side of *B*, and placed in a suitable position and at the proper height by a block or book, after fine threads have been passed through the eyelid, which is to be fixed over the cover-glass *E*, Fig. 2, previously gummed to the aperture. Over this is a second cover-glass represented by the interrupted line in *B*, Fig. 2, which is prevented from pressing on the membrane by a thin rim of putty or filter-paper placed on *B*. Between these two glasses and to their left the object can be kept moist with aqueous humour, fresh serum, or tepid salt solution. *B*, Fig. 2, also represents the membrane fixed to the pins and between the cover-slips.

With birds and small mammals *A* could be used instead of *B*, if the animal were desired to be examined from the opposite side, but the projecting arms would be in the way in the case of larger ones. In this event, of course, *A* would need to be similarly perforated for the pins to *B*.

This stage will necessitate two modifications in the mechanical arrangements of ordinary microscope-stands, but these will not interfere in any way with their usual efficiency, but will be simple and useful additions. One is the fixing of the stage to the stand so as to permit of the removal of half of the former, the other is the provision of a means of rotating the tube so as to allow of the study of different parts of the field[1].





[1] Mr Swift, of University Street, will make and supply the above-described, as well as the following simple apparatus, which I have called a *Live-development slide*, Figs. 3 and 4, because it permits of small living aquatic animals and larvæ being watched for hours or days, either as regards their circulation or growth, and also of the prolonged examination of the changes in the ova of fish or amphibia. It will also be of service in the study of small aquatic plants.

It consists of a 2·8 inch thick glass slide, 4 in. by 2 in., with an oval depression in its centre, from which run two grooves (or perforations if preferred) to either end of the slide. At the central end the grooves are somewhat enlarged, and at their outer ends are two tubular fittings, to which are connected rubber-tubings of corresponding small bore, one of which is the supply and the other the waste-pipe. A small perforated weight is attached to the supply-pipe, which is placed in a jug or tumbler which can be raised to increase the flow of water, if needed. A spring-catch may be affixed to either tube to prevent, as the case may be, either ingress or egress. The outlet tube may be placed between the lips, and the flow made more rapid by suction.

The omentum and mesentery, which require to be kept at their normal temperature, cannot be studied with this arrangement —as it can be used for birds, rabbits, or small dogs—but this matters the less, as the third eyelid of birds, the rabbit, the patagium, and the web of some birds, offer a sufficiently large field for observation and experimental inquiry in warm-blooded vertebrates. I have also thought out and shewn to Mr Hawksley a rough sketch of an arrangement by which the eyelid of a *non-anæsthetized* rabbit may be studied; but this will necessitate the use of the Czermak rabbit-holder, a transparent stage, and a horizontal position of the microscope.

Fig. 5 represents a simple arrangement for the purpose of making prolonged drawing less irksome, as it can be used in the *upright* position of the instrument, thus preventing the congestion of the head and eyes which too often result from the lengthened use of ordinary cameras, reflectors or prisms. To the cap which fits on to the eyepiece is attached a bracket carrying a frame into which is fitted a cover-slip or neutral-tint reflector. The joint connecting the frame and bracket permits of the inclination of the reflector to any desired angle, and rotation on a vertical axis is provided for, as the cap can be turned round on the eye-piece.

The observer's eye held at a little distance from the apparatus projects the reflected image through the reflector on to the drawing-pad, and the image and pencil are seen at the same time. Mr Swift makes the instrument.

THE DEVELOPMENT OF ELASMOBRANCH FISHES.

By F. M. BALFOUR, B.A. *Fellow of Trinity College, Cambridge.* (Plates XV. XVI. XVII. XVIII. XIX.)

Continued from p. 172.

External Epiblast.

THE change already alluded to in the previous section (p. 130) by which the external epiblast or epidermis becomes divided into two layers, is completed before the close of stage L.

In the tail region at this stage three distinct strata may be recognized in the epidermis. (1) An outer stratum of flattened horny cells, which fuse together to form an almost continuous membrane. (2) A middle stratum of irregular partly rounded and partly flattened cells. (3) An internal stratum of columnar cells, bounded towards the mesoblast by a distinct basement membrane (Pl. XV. fig. 8), unquestionably pertaining to the epiblast. This layer is especially thickened in the terminal parts of the paired fins (Pl. XV. fig. 1). The two former of these strata together constitute the epidermic layer of the skin, and the latter the mucous layer.

In the anterior parts of the body during stage L the skin only presents two distinct strata, viz. an inner somewhat irregular layer of rounded cells, the mucous layer, and an outer layer of flattened cells (Pl. XV. fig. 8).

The remaining history of the external epiblast, consisting as it does of a record of the gradual increase in thickness of the epidermic strata, and a topographical description of its variations in structure and thickness in different parts, is of no special interest and need not detain us here.

In the late embryonic periods subsequent to stage Q the layers of the skin cease to be so distinct as at an earlier period, partly owing to the innermost layer becoming less columnar, and partly to the presence of a large number of mucous cells, which have by that stage made their appearance.

I have followed with some care the development of the placoid scales, but my observations so completely accord with

those of Dr O. Hertwig[1], that it is not necessary to record them. The so-called enamel layer is a simple product of the thickening and calcification of the basement membrane, and since this membrane is derived from the mucous layer of epidermis, the enamel is clearly to be viewed as an epidermic product. There is no indication of a gradual conversion of the bases of the columnar cells forming the mucous layer of the epidermis into enamel prisms, as is frequently stated to occur in the formation of the enamel of the teeth in higher vertebrates.

Lateral line.

The lateral line and the nervous structures appended to it have been recently studied from an embryological point of view by Götte[2] in Amphibians and by Semper[3] in Elasmobranchs.

The most important morphological result which these two distinguished investigators believe themselves to have arrived at is the direct derivation of the lateral nerve from the ectoderm. On this point there is a complete accord between them, and Semper especially explains that it is extremely easy to establish the fact.

As will appear from the sequel, I have not been so fortunate as Semper in elucidating the origin of the lateral nerve, and my observations bear an interpretation not in the least in accordance with the views of my predecessors, though not perhaps quite conclusive against them.

It must be premised that two distinct structures have to be dealt with, viz. the *lateral line* formed of modified epidermis, and the *lateral nerve* whose origin is in question.

The lateral line is the first of the two to make its appearance, at a stage slightly subsequent to K, in the form of a linear thickening of the inner row of cells of the external epiblast, on each side, at the level of the notochord.

This thickening, in my youngest embryo in which it is found, has but a very small longitudinal extension, being

[1] *Jenaische Zeitschrift*, Vol. VIII.
[2] *Entwicklungsgeschichte d. Unke.*
[3] *Urogenital-system d. Selachier.* Semper's *Arbeiten*, Bd. II.

present through about 10 thin sections in the last part of the head and first part of the trunk. The thickening, though short, is very broad, measuring about 0·28 Mm. in transverse section, and presents no signs of a commencing differentiation of nervous structures. The large intestinal branch of the vagus can be seen in all the anterior sections in close contact with this line, and appears to me to give off to it posteriorly a small special branch which can be traced through a few sections, vide Pl. xv. fig. 2 *n.l.* But this branch is not sufficiently well marked to enable me to be certain of its real character. In any case the posterior part of the lateral line *is absolutely without any adjoining nervous structures or traces of such.*

The rudiment of the epidermic part of the lateral line is formed of specially elongated cells of the mucous layer of the epiblast, but around the bases of these certain rounder cells of a somewhat curious appearance are intercalated.

There is between this and my next youngest embryo an unfortunately large gap with reference to the lateral line, although in almost every other respect the two embryos might be regarded as belonging to the same stage. The lateral line in the older embryo extends from the hind part of the head to a point well behind the anus, and is accompanied by a nerve for at least two-thirds of its length.

In the foremost section in which it appears the intestinal branch of the vagus is situated not far from it, *and may be seen at intervals giving off branches to it.* There is no sign that these are otherwise than perfectly normal branches of the vagus. Near the level of the last visceral cleft the intestinal branch of the vagus gives off a fair-sized branch, which from the first occupies a position close to the lateral line though well within the mesoblast (Pl. xv. fig. 3*a*). This branch is the lateral nerve, and though somewhat larger, is otherwise much like the nerve I fancied I could see originating from the intestinal branch of the vagus during the previous stage.

It rapidly thins out posteriorly and also approaches closer and closer to the lateral line. At the front end of the trunk it is quite in contact with it, and a short way behind this region the cells of the lateral line arrange themselves in a gable-like form, in the angle of which the nerve is situated (Pl. xv.

fig. 3*b*, and 3*c*). In this position the nerve though small is still very distinct in all good sections, and is formed of a rod of protoplasm, with scattered nuclei, in which I could not detect a distinct indication of cell-areas. The hinder part of the nerve becomes continually smaller and smaller, without however presenting any indication of becoming fused with the epiblast, and eventually ceases to be visible some considerable distance in front of the posterior end of the lateral line.

The lateral line itself presents some points of not inconsiderable interest. In the first place, it is very narrow anteriorly and throughout the greater part of its length, but widens out at its hinder end, and is widest of all at its termination, which is perfectly abrupt. The following measurements of it were taken from an embryo belonging to stage L, which though not quite my second youngest embryo is only slightly older. At its hinder end it was 0·17 Mm. broad. At a point not far from this it was 0·09 Mm. broad, and anteriorly it was 0·05 Mm. broad. These measurements clearly show that the lateral line is broadest at what may be called its growing-point, a fact which explains its extraordinary breadth in the anterior part of the body at my first stage, viz. 0·28 Mm., a breadth which strangely contrasts with the breadth, viz. 0·05 Mm., which it has in the same part of the body at the present stage.

It still continues to form a linear area of modified epidermis, and has no segmental characters. Anteriorly it is formed by the cells of mucous layer becoming more columnar (Pl. XV. fig. 3*a*). In its middle region the cells of the mucous layer in it are still simply elongated, but, as has been said above, have a gable-like arrangement, so as partially to enclose the nerve (Pl. XV. fig. 3*b*). Nearer the hind end of the trunk a space appears in it between its columnar cells and the flattened cells of the outermost layer of the skin (Pl. XV. fig. 3*c*), and this space becomes posteriorly invested by a very definite layer of cells. The space (Pl. XV. fig. 3*d*) or lumen has a slit-like section, and is not formed by the closing in of an originally open groove, but by the formation of a cavity in the midst of the cells of the lateral line. Its walls are formed by a layer of columnar cells on the inner side, and flattened cells on the outer side, both layers however appearing to be derived from

the mucous layer of the epidermis. The outer layer of cells attains its greatest thickness dorsally.

During stages M, N, O, the lateral nerve gradually passes inwards into the connective tissue between the dorso-lateral and the ventro-lateral muscles, and becomes even before the close of stage N completely isolated from the lateral line.

The growth of the lateral line itself remains for some time almost stationary; anteriorly the cells retain the gable-like arrangement which characterised them at an earlier period, but cease to enclose the nerve; posteriorly the line retains its original more complicated constitution as a closed canal. In stage O the cells of the anterior part of the line, as well as those of the posterior, commence to assume a tubular arrangement, and the lateral line takes the form of a canal. The tubular form is due to a hollowing out of the lateral line itself and a rearrangement of its cells.

In stage P the first indication of segmental apertures to the exterior make their appearance, vide Pl. XV. fig. 4. The lateral line forms a canal situated completely below the skin, but at intervals (corresponding with segments) sends upwards and outwards prolongations towards the exterior. These prolongations do not during stage P acquire external openings. As is shown in my figure, a special area of the inner border of the canal of the lateral line becomes distinguished by its structure from the remainder.

No account of the lateral line would be complete without some allusion to the similar sensory structures which have such a wide distribution on the heads of Elasmobranchs; and this is especially important in the present instance, owing to the light thrown by a study of their development on the origin of the nerves which supply the sense-organs of this class. The so-called mucous canals of the head originate in the same way as does the lateral line; they are products of the mucous layer of the epidermis. They eventually form either canals with numerous openings to the exterior, or isolated tubes with terminal ampulliform dilatations.

I have not definitely determined whether the canal-system of the head arises in connection with the lateral line, or only eventually becomes so connected. The important point to be

noticed is, that at first no nervous structures are to be seen in connection with it. In stage O nerves for the mucous canals make their appearance as delicate branches of the main stems. These nerve-stems are very much ramified, and their branches have, in a large number of instances, an obvious tendency towards a particular sense-organ (Pl. XV. figs. 5 and 6).

I have not during stage O been able to detect a case of direct continuity between the two. This is, however, established in the succeeding stage P, in the case of the canals, and the facility with which it may be observed would probably render the embryo Elasmobranch a very favourable object for studying the connection between nerves and terminal sense-organs. The nerve (Pl. XV. fig. 7) dilates somewhat before uniting with the sense-organ, and the protoplasm of the nerve and the sense-organ become completely fused. The basement membrane of the skin is not continuous across their point of junction, and appears to unite with a delicate membrane-like structure, which invests the termination of the nerve. The ampullæ would seem to receive their nervous supply somewhat later than the canals, and the terminal swellings of the nerves supplying them are larger than in the case of the canals, and the connection between the ampullæ and the nerves not so clear. In the case of the head, there can for Elasmobranchs be hardly a question that the nerves which supply the mucous canals grow centrifugally from the original cranial nerve-stems, and do not originate in a peripheral manner from the integument.

This is an important point to make certain of in settling any doubtful features in the nervous supply of the lateral line. Professor Semper[1], with whom as dealing with Elasmobranchs we are more directly concerned, makes the following statement: "At the time when at the front end the lateral nerve has already completely separated itself from the ectoderm, and is situated amongst the muscles, it still lies in the middle of the body close to the ectoderm, and at the hind end of the body is not yet completely segmented off (abgegliedert) from the ectoderm." Although the last sentence of this quotation may seem to be opposed to my statements, yet it appears to me

[1] *Loc. cit.* p. 398.

probable that Professor Semper has merely seen the lateral nerve partially enclosed in the ectoderm. This position of the nerve no doubt affords a *presumption, but only a presumption,* in favour of a direct origin of the lateral nerve from the ectoderm; but against this interpretation of it are the following facts:

(1) That the front part of the lateral line is undoubtedly supplied by branches which arise in the ordinary way from the intestinal branch of the vagus; and we should not expect to find part of the lateral line supplied by nerves which originate in one way, and the remainder supplied by a nerve having a completely different and abnormal mode of origin.

(2) The growth of the lateral line is quite independent of that of the lateral nerve: the latter arises subsequently to the lateral line, and, so far as is shown by the inconclusive observation of my earliest stage, as an offshoot from the intestinal branch of the vagus; and though it grows along at first in close contact with the lateral nerve, yet it never presents, so far as I have seen, any indubitable indication of becoming split off from this, or of fusing with it.

(3) The fact that the cranial representatives of the lateral line are supplied with nerves which originate in the normal way[1], affords a strong argument in favour of the lateral line receiving an ordinary nerve-supply.

Considering all these facts, I am led to the conclusion *that the lateral nerve in Elasmobranchs arises as a branch of the vagus, and not as a direct product of the external epiblast.*

An interesting feature about the lateral line and the similar cephalic structures, is the fact of these being the only sense organs in Elasmobranchs which originate entirely from the mucous layer of the epiblast. This, coupled with the well-known facts about the Amphibian epiblast, and the fact that the mucous canals are the only sense-organs which originate subsequently to the distinct differentiation of the epiblast into mucous and horny layers, goes far to prove[2] that the mucous layer

[1] Götte extends his statements about the lateral nerve to the nerves supplying the mucous canals in the head; but my observations appear to me, as far as Elasmobranchs are concerned, nearly conclusive against such a derivation of the nerves in the head.

[2] I believe that Götte, amongst his very numerous valuable remarks in the *Entwicklungsgeschichte der Unke*, has put forward a view similar to this, though I cannot put my hand on the reference.

is to be regarded as the active layer of the epiblast, and that after this has become differentiated, an organ formed from the epiblast is always a product of it.

Muscle-Plates.

The muscle-plates at the close of stage K were flattened angular bodies with the apex directed forwards, their ventral edge being opposite the segmental duct, and their dorsal edge on a level with the middle of the spinal cord. They were composed of two layers, formed for the most part of columnar cells, but a small part of their splanchnic layer opposite the notochord had already become differentiated into longitudinal muscles.

During stage L the growth of these plates is very rapid, and their upper ends extend to the summit of the neural canal, and their lower ones nearly meet in the median ventral line. The original band of muscles (Pl. v. fig. 8 *m. p'*), whose growth was so slow during stages I and K, now increases with great rapidity, and forms the nucleus of the whole voluntary muscular system. It extends upwards and downwards by the continuous conversion of fresh cells of the splanchnic layer into muscle-cells. At the same time it grows rapidly in thickness, but it requires some little patience and care to unravel the details of this growth; and it will be necessary to enter on a slight digression as to the relations of the muscle-plates to the surrounding connective tissue.

As the muscle-plates grow dorsalwards and ventralwards their ends dive into the general connective tissue, whose origin has already been described (Pl. xv. fig. 1). At the same time the connective-tissue cells, which by this process become situated between the ends of the muscle-plates and the skin, grow upwards and downwards, and gradually form a complete layer separating the muscle-plates from the skin. The cells forming the ends of the muscle-plates retain unaltered their primitive undifferentiated character, and the separation between them and the surrounding connective-tissue cells is very marked. This however ceases to be the case in the parts of the muscle-plates on a level with the notochord and lower part of the

medullary canal; the thinnest sections and most careful examination are needed to elucidate the changes taking place in this region. The cells which form the somatic layer of the muscle-plates then begin to elongate and become converted into muscle-cells, at the same time that they are increasing in number to meet the rapid demands upon them. One result of these changes is the loss of the original clearness in the external boundary between the muscle-plates and the adjoining connective-tissue cells, which is only in exceptional cases to be seen so distinctly as it may be in Pl. XV. fig. 1 and 8. Longitudinal horizontal sections are the most instructive for studying the growth of the muscles, but transverse sections are also needed. The interpretation of the transverse ones is however rendered difficult, both by rapid alterations in the thickness of the connective-tissue layer between the skin and the muscle-plates (shown in Pl. XV. fig. 8), and by the angular shape of the muscle-plates themselves.

A careful study of both longitudinal and transverse sections has enabled me to satisfy myself of the fact that the cells of the somatic layer of the protovertebræ, equally with the cells of the splanchnic layer, are converted into muscle-cells, and some of these are represented in the act of undergoing this conversion in Pl. XV. fig. 8; but the difficulty of distinguishing the outline of the somatic layer of the muscle-plates, at the time its cells become converted into muscle-cells, renders it very difficult to determine whether any cells of this layer join the surrounding connective tissue. General considerations certainly lead me to think that they do not; but my observations do not definitely settle the point.

From these facts it is clear, as was briefly stated in the last chapter, *that both layers of the muscle-plate are concerned in forming the great lateral muscle, though the splanchnic layer is converted into muscles very much sooner than the somatic*[1].

[1] The difference between Dr Götte's account of the development of the muscles and my own consists mainly in my attributing to the somatic layer of the muscle-plates a share in the formation of the great lateral muscles, which he denies to it. In the last part of this Monograph, *Journal of Anat. and Phys.* Vol. XI. pp. 146—8, too much stress was unintentionally laid on the divergence of our views; a divergence which appears to have, in part at least, arisen, not from our observations being opposed, but from Dr Götte's having taken the highly differentiated Bombinator as his type instead of the less differentiated Elasmobranch.

The remainder of the history of the muscle-plates presents no points of special interest.

Till the close of stage L, the muscle-plates are not distinctly divided into dorsal and ventral segments, but this division, which is so characteristic of the adult, commences to manifest itself during stage M, and is quite completed in the succeeding stage. It is effected by the appearance, nearly opposite the lateral line, of a layer of connective tissue which divides the muscles on each side into a dorso-lateral and ventro-lateral section. Even during stage O the ends of the muscle-plate are formed of undifferentiated columnar cells. The peculiar outlines of the intermuscular septa gradually appear during the later stages of development, causing the well-known appearances of the muscles in transverse sections, but require no special notice here.

With reference to the histological features of the development of the muscle-fibres, I have not pushed my investigations very far. The primitive cells present the ordinary division, well known since Remak, into a striated portion and a non-striated portion, and in the latter a nucleus is to be seen which soon undergoes division and gives rise to several nuclei in the non-striated part, while the striated part of each cell becomes divided up into a number of fibrillæ. I have not however determined what exact relation the original cells hold to the eventual primitive bundles, or anything with reference to the development of the sarcolemma.

The Muscles of the Limbs.—These are formed during stage O coincidently with the cartilaginous skeleton, in the form of two bands of longitudinal fibres on the dorsal and ventral surfaces of the limbs. Dr Kleinenberg first called my attention to the fact that he had proved the limb-muscles in *Lacerta* to be derived from the muscle-plates. This I at first believed did not hold good for Elasmobranchs, but have since determined that it does so. Between stages K and L the muscle-plates grow downwards as far as the limbs and then turn outwards and grow into them. Small portions of several muscle-plates come in this way to be situated in the limbs, and are very soon segmented off from the remainder of the muscle-plates. The portions of muscle-plates thus introduced into the limbs soon lose their original distinctness, and can no longer be recognised

in stage L. There can however be but little doubt that they supply the tissue for the muscles of the limbs. The muscle-plates themselves after giving off these buds to the limbs grow downwards, and by stage L cease to show any trace of what has occurred (Pl. xv. fig. 1). This fact, coupled with the late development of the muscles of the limbs (stage O), caused me to fall into my original error.

The Vertebral Column and Notochord.

In the October number of the *Journal* an account was given of the origin of the tissue destined to form the vertebral bodies; it merely remains to describe the changes undergone by this in becoming converted into the permanent vertebræ.

This subject has already been dealt with by a considerable number of anatomists, and my investigations coincide in the main with the results of my predecessors. Especially the researches of Gegenbaur[1] may be singled out as containing the pith of the whole subject, and my results, while agreeing in all but minor points with his, do not supplement them to any very great extent. I cannot do more than confirm Götte's[2] account of the development of the hæmal arches, and may add that Cartier[3] has given a good account of the later development of the centra. Under the circumstances it has not appeared to me to be worth while recording with great detail my investigations; but I hope to be able to give a somewhat more complete history of the whole subject than has appeared in any single previous memoir.

At their first appearance the cells destined to form the permanent vertebræ present the same segmentation as the muscle-plates. This segmentation soon disappears, and between stages K and L the tissue of the vertebral column forms a continuous investment of the notochord which cannot be distinguished from the adjoining connective tissue. Immediately surrounding the notochord a layer formed of a single row of cells may be observed, which is not however very distinctly marked[4].

[1] *Das Kopfskelet d. Selachier*, p. 123.
[2] *Entwicklungsgeschichte d. Unke*, p. 433-4.
[3] *Zeitschrift f. Wiss. Anat.* Bd. xxv., Supplement.
[4] Vide Self, *Journal of Anat. and Phys.*, Vol. xi. p. 169.

During the stage L there appear four special concentrations of mesoblastic tissue adjoining the notochord, two of them dorsal and two of them ventral. They are not segmented, and form four ridges seated on the sides of the notochord. They are united with each other by a delicate layer of tissue, and constitute the rudiments of the neural and hæmal arches. In longitudinal sections of stage L special concentrated wedge-shaped masses of tissue are to be seen between the muscle-plates, which must not be confused with these rudiments. Immediately around the notochord the delicate investment of cells previously mentioned, is still present.

The rudiments of the arches increase in size and distinctness in the succeeding stages, and by stage N have unquestionably assumed the constitution of embryonic cartilage. In the meantime there has appeared surrounding the sheath of the notochord a well-marked layer of tissue which stains deeply with hæmatoxylin, and with the highest power may be observed to contain flattened nuclei. It is barely thicker than the adjoining sheath, but is nevertheless the rudiment of vertebral bodies. Pl. XV. fig. 9, *vb*. Whence does this layer arise? To this question I cannot give a quite satisfactory answer. It is natural to conclude that it is derived from the previously existing mesoblastic investment of the notochord, but in the case of the vertebral column I have not been able to prove this. Observations on the base of the brain afford fairly conclusive evidence that the homologous tissue present there has this origin. Gegenbaur apparently answers the question of the origin of this layer in the way suggested above, and gives a figure in support of his conclusion (Pl. XXII. fig. 3)[1].

The layer of tissue which forms the vertebral bodies rapidly increases in thickness, and very soon, at a somewhat earlier period than represented in Gegenbaur's Plate XXII. fig. 4, a distinct membrane (Kölliker's Membrana Elastica Externa) may easily be recognised surrounding it and separating it

[1] None of my specimens resembles this figure, and the layer when first formed is in my embryos much thinner than represented by Gegenbaur, and the histological structure of the embryonic cartilage is very different from that of the cartilage in the figures alluded to. Götte's very valuable researches with reference to the origin of this layer in Amphibians tend to confirm the view advocated in the text.

from the adjoining tissue of the arches. Gegenbaur's figure gives an excellent representation of the appearance of this layer at the period under consideration. It is formed of a homogeneous basis containing elongated concentrically arranged nuclei, and constitutes a uniform unsegmented investment for the notochord (vide Pl. XV. fig. 10).

The neural and hæmal arches now either cease altogether to be united with each other by a layer of embryonic cartilage, or else the layer uniting them is so delicate that it cannot be recognised as true cartilage. They have moreover by stage P undergone a series of important changes. The tissue of the neural arches does not any longer form a continuous sheet, but is divided into (1) a series of arches encircling the spinal cord, and (2) a basal portion resting on the cartilaginous sheath of the notochord. There are two arches to each muscle-plate, one continuous with the basal portion of the arch-tissue and forming the true arch, which springs opposite the centre of a vertebral body, and the second not so continuous, which forms what is usually known as the intercalated piece. Between every pair of true arches the two roots of a single spinal nerve pass out. The anterior root passes out in front of an intercalated piece and the posterior behind it[1].

The basal portion of the arch-tissue likewise undergoes differentiation into a vertebral part continuous with the true arch and formed of hyaline cartilage, and an intervertebral segment formed of a more fibrous tissue.

The hæmal arches, like the neural arches, become divided into a layer of tissue adjoining the cartilaginous sheath of the notochord, and processes springing out from this opposite the centres of the vertebræ. These processes throughout the region of the trunk in front of the anus pass into the space between the dorsal and ventral muscles, and are to be regarded as rudiments of ribs. The tissue with which they are continuous, which is exactly equivalent to the tissue from which the neural arches originate, is not truly a part of the rib. In the tail, behind the anus and kidneys, the cardinal

[1] In the adult Scyllium it is well known that the posterior root pierces the intercalated cartilage and the anterior root the true neural arch. This however does not seem to be the case in the embryo at stage P.

veins fuse to form an impaired caudal vein below the aorta, and in this part a fresh series of processes originates on each side from the hæmal tissue adjoining the cartilaginous sheath of the notochord, and eventually, by the junction of the processes of the two sides, a canal which contains the aorta and caudal vein is formed below the notochord. These processes for a few segments coexist with small ribs (vide Pl. xv. fig. 10), a fact which shows (1) that they cannot be regarded as modified ribs, and (2) that the tissue from which they spring is to be viewed as a kind of general basis for all the hæmal processes which may arise, and is not specially connected with any one set of processes.

While these changes (all of which are effected during stage P) are taking place in the arches, the tissue of the vertebral bodies or cartilaginous investment of the notochord, though much thicker than before, still remains as a continuous tube whose wall exhibits no segmental differentiations.

It is in stage Q that these differentiations first appear in the vertebral regions opposite the origin of the neural arches. The outermost part of the cartilage at these points becomes hyaline and almost undistinguishable in structure from the tissue of the arches[1]. These patches of hyaline cartilage grow larger and cause the vertebral parts of the column to constrict the notochord, whilst the intervertebral parts remain more passive, but become composed of cells with very little intercellular substance. Coincidently also with these changes, part of the layer internal to the hyaline cartilage becomes modified to form a somewhat peculiar tissue, the intercellular substance of which does not stain, and in which calcification eventually arises (Pl. xv. fig. 11). The innermost layer adjoining the notochord retains its primitive fibrous character, and is distinguishable as a separate layer through both the vertebral and the intervertebral regions. As a result of these changes a transverse section through the centre of the vertebral regions now exhibits three successive rings (vide Pl. xv. fig. 11), an external ring of hyaline cartilage invested by 'the membrana elastica externa' (*m.el*), followed by a

[1] A good representation of a longitudinal section at this stage is given by Cartier (*Zeitschrift f. Wiss. Zoologie*, Bd. xxv., Supplement Pl. iv. fig. 1), who also gives a fair description of the succeeding changes of the vertebral column.

ring of calcifying cartilage, and internal to this a ring of fibrous cartilage, which adjoins the now slightly constricted notochord. A transverse section of an intervertebral region shows only a thick outer and thin inner ring of fibrous cartilage, the latter in contact with the sheath of the unconstricted notochord.

The constriction of the notochord proceeds till in the centre of the vertebræ it merely forms a fibrous band. The tissue internal to the calcifying cartilage then becomes hyaline, so that there is formed in the centre of each vertebral body a ring of hyaline cartilage immediately surrounding the fibrous band which connects the two unconstricted segments of the notochord. The intervertebral tissue becomes more and more fibrous. In Cartier's paper before quoted there is a figure (fig. 3) which represents the appearance presented by a longitudinal section of the vertebral column at this stage.

The relation of the vertebral bodies to the arches requires a short notice. The vertebral hyaline cartilage becomes almost precisely similar to the tissue of the arches, and the result is, that were it not for the 'membrana elastica externa' it would be hardly possible to distinguish the limits of the two tissues. This membrane however persists till the hyaline cartilage has become a very thick layer (Pl. xv. fig. 11), but I have failed to detect it in the adult, so that I cannot there clearly distinguish the arches from the body of the vertebræ. From a comparison however of the adult with the embryo, it is clear that the arches at most form but a small part of what is usually spoken of as the body of the vertebræ.

The changes in the notochord itself during the stages subsequent to K are not of great importance. The central part retains for some time its previous structure, being formed of large vacuolated cells with an occasional triangular patch of protoplasm containing the starved nucleus and invested by indurated layers of protoplasm. These indurated layers are all fused, and are probably rightly regarded by Gegenbaur and Götte as representing a sparse intercellular matter. The external protoplasmic layer of the notochord ceases shortly after stage K to exhibit any traces of a division into separate cells, but forms a continuous layer with irregular prominences and numerous nuclei (Pl. xv. fig. 9). In the stages subsequent

to P further changes take place in the notochord: the remains of the cells become more scanty and the intercellular tissue assumes a radiating arrangement, giving to sections of the notochord the appearance of a number of lines radiating from the centre to the periphery (Pl. XV. fig. 11).

The sheath of the notochord grows in thickness, and during stage L there is no difficulty in seeing in it the fine radial markings already noticed by Müller[1] and Gegenbaur[2], and regarded by them as indicating pores. Closely investing the sheath of the notochord there is to be seen a distinct membrane, which, though as a rule closely adherent to the sheath, in some examples separates itself from it. It is perhaps the membrane identified by W. Müller[3] (though not by Gegenbaur) as Kölliker's 'membrana elastica interna.' After the formation of the cartilaginous investment of the notochord, this membrane becomes more difficult to see than in the earlier stage, though I still fancy that I have been able to detect it. The sheath of notochord also appears to me to become thinner, and its radial striation is certainly less easy to detect[4].

[1] *Jenaische Zeitschrift*, Vol. VI. [2] *Loc. cit.* [3] *Loc. cit.*
[4] Gegenbaur makes the reserve statement with reference to the sheath of the notochord. For my own sections the statement in the text certainly holds good. Fortunately the point is one of no importance.

DEVELOPMENT OF THE SPINAL NERVES AND OF THE SYMPATHETIC NERVOUS SYSTEM.

The spinal nerves.—The development of the spinal nerves has been already treated by me at considerable length in a paper read before the Royal Society in December, 1875[1], and I have but little fresh matter to add to the facts narrated in that paper. The succeeding account, though fairly complete, is much less full than the previous one in the *Philosophical Transactions*, but a number of morphological considerations bearing on this subject are discussed.

The rudiments of the posterior roots make their appearance considerably before those of the anterior roots. They arise during stage I, as outgrowths from the spinal cord, at a time when the muscle-plates do not extend beyond a third of the way up the sides of the spinal cord, and in a part where no scattered mesoblast-cells are present. They are formed first in the anterior part of the body and successively in the posterior parts, in the following way. At a point where a spinal nerve is about to arise, the cells of the dorsal part of the cord begin to proliferate, and the uniform outline of the cord becomes broken (Pl. XVI. fig. 3). There is formed in this way a small prominence of cells springing from the summit of the spinal cord, and constituting a rudiment of a pair of posterior roots. In sections anterior to the point where a nerve is about to appear, the nerve-rudiments are always very distinctly formed. Such a section is shown in Pl. XVI. fig. 2, and the rudiments may there be seen as two club-shaped masses of cells, which have grown outwards and downwards from the extreme dorsal summit of the neural canal and in contact with its walls. The rudiments of the two sides meet at their point of origin at the dorsal median line, and are dorsally perfectly continuous with the walls of the canal.

[1] *Phil. Trans.* Vol. 166, p. 175.

It is a remarkable fact that rudiments of posterior roots are to be seen in every section. This may be interpreted as meaning that the rudiments are in very close contact with each other, but more probably means, as I hope to show in the sequel, that there arises from the spinal cord a continuous outgrowth from which discontinuous processes (the rudiments of posterior roots) grow out.

After their first formation these rudiments grow rapidly ventralwards in close contact with the spinal cord (vide Pl. XVI. fig. 1, and Vol. XI. Pl. V. figs. 6 and 7), but soon meet with and become partially enclosed in the mesoblastic tissue (Vol. XI. Pl. V. fig. 7). The similarity of the mesoblast and nerve-tissue in Scyllium and Pristiurus embryos hardened in picric or chromic acid, render the nerves in these genera, at the stage when they first become enveloped in mesoblast, difficult objects to observe; but no similar difficulty is encountered in the case of Torpedo embryos.

While the rudiments of the posterior roots are still quite short, those of the anterior roots make their first appearance. Each of these (Pl. XVI. fig. 4 *a.r.*) arises as a very small but distinct conical outgrowth from a ventral corner of the spinal cord. From the very first the rudiments of the anterior roots have an indistinct form of peripheral termination and somewhat fibrous appearance, while the protoplasm of which they are composed becomes attenuated towards its end. The points of origin of the anterior roots from the spinal cord are separated by considerable intervals. In this fact, and also in the fact of the nerves of the two sides never being united with each other in the median line, the anterior roots exhibit a marked contrast to the posterior. There are thus constituted, before the close of stage I, the rudiments of both the anterior and posterior roots of the spinal nerves. The rudiments of both of these take their origin from the involuted epiblast of the neural canal, and the two roots of each spinal nerve are at first quite unconnected with each other. It is scarcely necessary to state that the pairs of roots correspond in number with the muscle-plates.

It is not my intention to enter with any detail into the subsequent changes of the rudiments whose origin has been described, but a few points especially connected with their

early development are sufficiently important to call for attention.

One feature of the posterior roots at their first formation is the fact that they appear as processes of a continuous outgrowth of the spinal cord. This state of affairs is not of long continuance, and before the close of stage I each posterior root has a separate junction with the spinal cord. What then becomes of the originally continuous outgrowth? It has not been possible for me to trace the fate of this step by step; but the discovery that at a slightly later period (stage K) there is present a continuous commissure independent of the spinal cord, which connects the dorsal and central extremities of all the spinal nerves, renders it very probable that the original continuous outgrowth becomes converted into this commissure. Like all the other nervous structures, this commissure is far more easily seen in embryos hardened in a mixture of osmic and chromic acids or osmic acid, than in those hardened in picric acid. Its existence must be regarded as one of the most remarkable results of my researches upon the Elasmobranch nervous system. At stage K it is fairly thick, though it becomes much thinner at a slightly later period. Its condition during stage K is shown in Vol. XI. Plate VI. fig. 18, *com.* What it has been possible for me to make out of its eventual fate is mentioned subsequently[1].

A second feature of the earliest condition of the posterior roots is their attachment to the extreme dorsal summit of the spinal cord—a point of attachment very different from that which they eventually acquire. Before the commencement of stage K this state of things has become altered; and the posterior roots spring from the spinal cord in the position normal for Vertebrates.

This apparent migration caused me at first great perplexity, and I do not feel quite satisfied that I have yet got completely to the bottom of its meaning. The explanation which appears to me most probable has suggested itself in the course of some observations on the development of the thin roof of the fourth

[1] It is not by any means always possible to detect this commissure in transverse sections. As I have suggested, in connection with a similar commissure connecting the vagus branches, it perhaps easily falls out of the section, and is always so small that the hole left would certainly be invisible.

ventricle. A growth of cells appears to take place in the median dorsal line of the roof of the spinal cord. This growth tends to divaricate the two lateral parts of the cord, which are originally contiguous in the dorsal line, and causes therefore the posterior roots, which at first spring from the dorsal summit, to assume an apparent attachment to the side of the cord at some little distance from the summit. If this is the true explanation of the change of position which takes place, it must be regarded as due rather to peculiar growths in the spinal cord, than to any alteration in the absolute attachment of the nerves.

By stage K the rudiment of the posterior root has become greatly elongated, and exhibits a division into three distinct portions (Pl. XVI. fig. 6):

(1) A proximal portion, in which is situated the pedicle of attachment to the wall of the neural canal.

(2) an enlarged portion, which may conveniently from its future fate be called the spinal ganglion.

(3) a distal portion beyond this.

The proximal portion presents a fairly uniform diameter, and ends dorsally in a rounded expansion; it is attached, remarkably enough, *not by its extremity, but by its side, to the spinal cord. The dorsal extremities of the posterior roots are therefore free.* It seems almost certain that the free dorsal extremities of these roots serve as the starting points for the dorsal commissure before mentioned, which connects the roots together. The attachment of the posterior nerve-root to the spinal cord is, on account of its small size, very difficult to observe. In favourable specimens there may however be seen a distinct cellular prominence from the spinal cord, which becomes continuous with a small prominence on the lateral border of the nerve-root near its distal extremity. The proximal extremity of the rudiment is composed of cells, which, by their small size and circular form, are easily distinguished from those which form the succeeding or ganglionic portion of the nerve. This succeeding part has a swollen configuration, and is composed of large elongated cells with oval nuclei. The remainder of the rudiment forms the commencement of the true nerve.

The anterior root, which, at the close of stage I, formed a small and inconspicuous prominence from the spinal cord,

grows rapidly during the succeeding stages, and soon forms an elongated cellular structure with a wide attachment to the spinal cord (Pl. XVI. fig. 5). At first it passes obliquely and nearly horizontally outwards, but, before reaching the muscle-plate of its side, takes a bend downwards (Pl. XVI. fig. 7).

I have not definitely made out when the anterior and posterior roots unite, but this may easily be seen to take place before the close of stage K (vide Vol. XI. Pl. VI. fig. 18).

One feature of some interest with reference to the anterior roots, is the fact that they arise not vertically below, but alternately with the dorsal roots, a condition which persists in the adult.

Although I have made some efforts to determine the eventual fate of the commissure uniting the dorsal roots, these have not hitherto been crowned with success. It grows thinner and thinner, becoming at the same time composed of fibrous protoplasm with imbedded nuclei (Pl. XVI. fig. 8 and 9). By stage M it is so small as to be quite indistinguishable in transverse sections; and I have failed in stage P to recognize it at all. I can only conclude that it gradually atrophies, and finally vanishes without leaving a trace. Both its appearance and history are very remarkable, and deserve the careful attention of future investigators.

There can be little doubt that it is some sort of remnant of an ancestral structure in the nervous system; and it would appear to indicate that the central nervous system must originally have been formed of a median and two lateral strands. At the same time I very much doubt whether it can be brought into relation with the three rows of ganglion-cells (a median and two lateral) which are so frequently present on the ventral side of annelid nerve-cords.

My results may be summarized as follows:—Along the extreme dorsal summit of the spinal cord there arises on each side a continuous outgrowth. From each outgrowth processes corresponding in number to the muscle-plates grow downwards. These are the rudiments of the posterior nerve-roots. The outgrowths, though at first attached to the spinal cord throughout their whole length, soon cease to be so, and remain in connection with it at certain points only, which form the

primitive junctions of the posterior roots with the spinal cord. The original outgrowth on each side remains as a bridge, uniting together the dorsal extremities of all the posterior roots. The posterior roots, though primitively attached to the dorsal summit of the spinal cord, eventually come to arise from its sides. The original homogeneous rudiments before the close of stage K become differentiated into a root, a ganglion, and a nerve.

The anterior roots, like the posterior, are outgrowths from the spinal cord, but are united independently with it, and the points from which they spring originally, remain as those by which they are permanently attached. The anterior roots arise, not vertically below, but in the intervals between the posterior roots. They are at first quite separate from the posterior roots; but before the close of stage K a junction is effected between each posterior root and the corresponding anterior root. The anterior root joins the posterior at some little distance below its ganglion.

The results here arrived at are nearly in direct opposition to those of the majority of investigators, though in accordance, at least so far as the posterior roots are concerned, with the beautiful observations of Hensen 'on the Development of Mammalia[1].'

In the present number of this *Journal* there is a paper by Mr Marshall on the development of the nerves in Birds, in which the author shows in a most striking manner that the observations recorded here for Elasmobranchs hold good for the posterior roots of Birds. The similarity between his figures and my own is very noticeable. A further discussion of the literature would be quite unprofitable, and I proceed at once to certain considerations suggested by the above observations.

General considerations.—One point of general anatomy upon which my observations throw considerable light, is the *primitive origin of nerves.* So long as it was admitted that the spinal and cerebral nerves developed in the embryo independently of the central nervous system, their mode of origin always presented to my mind considerable difficulties. It never ap-

[1] *Zeit. f. Anat. u. Entwicklungsgeschichte*, Vol. I.

peared clear how it was possible for a state of things to have arisen in which the central nervous system as well as the peripheral terminations of nerves, whether motor or sensory, were formed independently of each other; while between them a third structure was developed, which, growing out either towards the centre or towards the periphery, ultimately brought the two into connection. That such a condition could be a primitive one seemed scarcely possible.

Still more remarkable did it appear, on the supposition that the primitive mode of formation of these parts was represented in the developmental history of Vertebrates, that we should find similar structural elements in the central and in the peripheral nervous systems. The central nervous system arises from the epiblast, and yet contains precisely similar nerve-cells and nerve-fibres to the peripheral nervous system, which, when derived from the mesoblast, was necessarily supposed to have an origin completely different from that of the central nervous system. Both of these difficulties are to a great extent removed by the facts of the development of these parts in Elasmobranchs.

It is possible to suppose that in their primitive differentiation contractile and sensory systems may, as in Hydra[1], have been developed from the protoplasm of even the same cell. As the sensory and motor systems became more complicated, the sensory portion of a cell would become separated by an increasing interval from the muscular part of a cell, and the two parts of a cell would only be connected by a long protoplasmic process. When such a condition as that was reached, the sensory portion of the cell would be called a ganglion-cell or terminal sensory organ, the connecting process a nerve, and the contractile portion of the cell a muscle-cell. When these organs were in this condition, it might not impossibly happen for the general developmental growth which tended to separate the ganglion-cell and the muscle-cell to be so rapid as to render it impossible for the growth of the connecting nerve to keep pace with it, and that thus the process connecting the ganglion-cell and the muscle-cell might become ruptured. Nevertheless the tendency of the process to grow from the ganglion cell to the

[1] Kleinenberg Hydra.

muscle-cell, would remain, and when the rapid developmental growth had ceased, the two would become united again by the growth of the process which had previously been ruptured. It will be seen that this hypothesis, which I have considered only with reference to a single nerve and muscle-cell, might be extended so as to apply to a complicated central nervous system and peripheral nerves and muscles, and also could apply equally as well to the sensory as to the motor terminations of a nerve. In the case of the sensory termination, we should only have to suppose that the centre nervous cell became more and more separated by the general growth from the recipient terminal sensory cell, and that during the general growth the connection between the two was mechanically ruptured but restored again on the termination of the more rapid growth.

As the descendants of the animal in which the rupture occurred became progressively more complicated, the two terminal cells must have become widely separated at a continually earlier period, till finally they may have been separated at a period of development when they were indistinguishable from the surrounding embryonic cells; and since the rupture would also occur at this period, the primitive junction between the nerve-centre and termination would escape detection. The object of this hypothesis is to explain the facts, so far as they are known, of the development of the nervous system in Vertebrates.

In Vertebrates we certainly appear to have an outgrowth from the nervous system, which eventually becomes united with the muscle or sensory terminal organs. The ingenious hypothetical scheme of development of the nerves given by Hensen[1] would be far preferable to the one suggested if it could be brought into conformity with the facts. There is, however, at present no evidence for Hensen's view, as he himself admits, but considering how little we know of the finer details of the development of nerves, it seems not impossible that such evidence may be eventually forthcoming. The evidence from my own observation is, so far as it goes, against it. At a time anterior to the outgrowth of the spinal

[1] Virchow's *Archiv*, Vol. XXXI. 1864.

nerves, I have shown[1] that the spinal cord is completely invested by a delicate hyaline membrane. It is difficult to believe that this is pierced by a number of fine processes, which completely escape detection, but which must, nevertheless, be present on the hypothesis of Hensen.

The facts of the development of nerves in Vertebrates are unquestionably still involved in considerable doubt. It may, I think, be considered as certain, that in Elasmobranchs the roots of the spinal and cranial nerves are outgrowths of the central nervous system. How the final terminations of the nerves are formed is, however, far from being settled. Götte[2], whose account of the development of the spinal ganglia is completely in accordance with the ordinary views, yet states[3] that the growth of the nerve-fibres themselves is a centrifugal one from the ganglia. My own investigations prove that the ganglia have a centrifugal development, and also appear to demonstrate that the nerves themselves near the ganglion have a similar manner of growth. Moreover, the account given in the preceding chapter of the manner in which the nerves become connected with the mucous canals of the head, goes far to prove that the whole growth of the nerves is a centrifugal one. The combination of all these converging observations tells strongly in favour of this view.

On the other hand, Calberla[4] believes that in the tails of larval Amphibians he has seen connective-tissue cells unite with nerve-processes, and become converted into nerves, but he admits that he cannot definitely prove that the axis-cylinder has not a centrifugal growth, while the connective-tissue cells merely become converted into the sheath of the nerve. If Calberla's view be adopted, that the nerves are developed directly out of a chain of originally indifferent cells, each cell of the chain being converted in turn into a section of the nerve, an altogether different origin of nerves from that I have just suggested would seem to be indicated.

The obvious difficulty, already alluded to, of understanding how it is, according to the generally accepted mode of development of the spinal nerves, that precisely similar nerve-cells and

[1] *Phil. Trans.*, 1876.
[2] *Entwicklungsgeschichte der Unke.*
[3] *Loc. cit.* p. 516.
[4] *Archiv für Micros. Anat.* Vol. XI. 1875.

nerves should arise in structures which have such different origins as the central nervous system and the spinal nerves, is completely removed if my statements on the development of the nerves in Elasmobranch represent the truth.

One point brought out in my investigations appears to me to have bearings upon the origin of the central canal of the vertebrate nervous system, and in consequence upon the origin of the vertebrate nervous system itself. This point is, that the posterior nerve-rudiments make their first appearance at the extreme dorsal summit of the spinal cord. The transverse section of the ventral nervous cord of an ordinary segmented Annelid consists of two symmetrical halves placed side by side. If by a mechanical folding the two lateral halves of the nervous cord became bent towards each other, while into the groove between the two the external skin became pushed, we should have an approximation to the vertebrate nervous system. Such a folding as this might take place to give extra rigidity to the body in the absence of a vertebral column.

If this folding were then completed in such a way that the groove, lined by external skin and situated between the two lateral columns of the nervous system, became converted into a canal, above and below which the two columns of the nervous system united, we should have in the transformed nervous cord an organ strongly resembling the spinal cord of Vertebrates.

It is well known that the nerve-cells are always situated on the ventral side of the abdominal nerve-cord of Annelids, either as a continuous layer, or in the former of two, or more usually, three bands. The dorsal side of the cord is composed of nerve-fibres or white matter. If the folding I have supposed were to take place in the Annelid nervous-cord, the grey and white matters would have very nearly the same relative situations as they have in the Vertebrate spinal cord. The grey matter would be situated in the interior and line the central canal, and the white matter would nearly surround the grey. The nerves would then arise, not from the sides of the nervous cord as in existing Annelids, but from its extreme ventral summit. One of the most striking features which I have brought to light with reference to the development of the posterior roots, is the fact of their growing out from the extreme dorsal summit of the

neural canal, a position analogous to the ventral summit of the Annelidan nervous cord. Thus the posterior roots of the nerves in Elasmobranchs[1] arise, in the exact manner which might have been anticipated, were the spinal canal due to such a folding as I have suggested.

The argument from the position of the outgrowth of nerves becomes the more striking from its great peculiarity, and forms a feature which would be most perplexing without some such explanation as I have proposed. The central epithelium of the neural canal, according to this view, represents the external skin, and its ciliation in certain cases may, perhaps, be explained as a remnant of the ciliation of the external skin still found amongst many of the lower Annelids.

I have employed the comparison of the Vertebrate and Annelidan nervous cords, not so much to prove a genetic relation between the two, as to show the *à priori* possibility of the formation of a spinal cord, and the *à posteriori* evidence we have of the vertebrate canal having been formed in the way indicated. I have not made use of what is really my strongest argument, viz. that the embryological mode of formation of the spinal canal by a folding in of the external epiblast is the very method by which I supposed the spinal canal to have been formed in the ancestors of Vertebrates. My object has been to suggest a meaning for the peculiar primitive position of the posterior roots, rather than to attempt to explain in full the origin of the spinal canal.

Although the homologies between the Vertebrate and the Annelidan nervous systems are not necessarily involved in the questions which arise with reference to the formation of the spinal canal, they have nevertheless considerable bearings on it.

Two views have recently been put forward on this subject. Professor Gegenbaur[2] looks upon the central nervous system of Vertebrates as equivalent to the superior œsophageal ganglia

[1] There are strong reasons for regarding the posterior roots as the primitive ones. These I shall speak of later, but may state that they depend:

(1) On the fact that only *posterior* roots exist in the brain.
(2) That only posterior roots exist in Amphioxus.
(3) That the posterior roots develope at an earlier period than the anterior.

[2] *Grundriss d. Vergleichenden Anat.* p. 264.

of Annelids and Arthropods only, while Professors Leydig[1] and Semper[2] and Dr Dohrn[3] compare it with the whole Annelidan nervous system.

The first of these two views is only possible on the supposition that Vertebrates are descended from unsegmented ancestors, and even then presents considerable difficulties. If the ancestors of Vertebrates were segmented animals, and several of the recent researches tend to show that they were, they must almost certainly have possessed a nervous cord like that of existing Annelids. If such were the case, it is inconceivable that the greater portion of the nervous system which forms the ventral cord can have become lost, and the system reduced to the superior œsophageal ganglia. Dr Dohrn[4], who has speculated very profoundly on this matter, has attempted to explain and remove some of the difficulties which arise in comparing the nervous systems of Vertebrates and Annelids. He supposes that the segmented Annelids, from which Vertebrates are descended, were swimming animals. He further supposes that their alimentary canal was pierced by a number of gill-slits, and that the anterior amongst these served for the introduction of nutriment into the alimentary canal, in fact as supplementary mouths as well as for respiration. Eventually the old mouth and throat atrophied, and one pair of coalesced gill-slits came to serve as the sole mouth. Thus it came about that on the disappearance of that portion of the alimentary canal, which penetrated the œsophageal nervous ring, the latter structure ceased to be visible as such, and no part of the alimentary canal was any longer enclosed by a commissure of the central nervous system. With the change of mouth Dr Dohrn also supposes that there took place a change, which would for a swimming animal be one of no great difficulty, of the ventral for

[1] *Bau des thierischen Körpers.*

[2] *Stammesverwandschaft d. Wirbelthiere u. Wirbellosen* and *Die Verwandschaftsbeziehungen d. gegliederten Thiere.* This latter work, for a copy of which I return my best thanks to the author, came into my hands after what follows was written, and I much regret only to have been able to make one or two passing allusions to it. The work is a most important contribution to the questions about to be discussed, and contains a great deal that is very suggestive; some of the conclusions with reference to the Nervous System appear to me however to be directly opposed to the observations on Spinal Nerves above recorded.

[3] *Ursprung d. Wirbelthiere u. Princip des Functionswechsels.*

[4] *Loc. cit.*

the dorsal surface. This general explanation of Dr Dohrn's, apart from the considerable difficulty of the fresh mouth, appears to me to be fairly satisfactory. Dr Dohrn has not however in my opinion satisfactorily dealt with the questions of detail which arise in connection with this comparison. One of the most important points for his theory is to settle the position where the nervous system was formerly pierced by the œsophagus. This position he fixes in the fourth ventricle, and supports his hypothesis by the thinness of the roof of the spinal canal in this place, and the absence (?) of nervous structures in it.

It appears to me that this thinness cannot be used as an argument. In the first place, if the hypothesis I have suggested as to the formation of the spinal canal be accepted, the formation of the canal must be supposed to have occurred in point of time either after or before the loss of the primitive mouth. If, on the one hand, the spinal canal made its appearance before the atrophy of the primitive mouth, the folding to form it must necessarily have ceased behind the mouth; and, on the supposition of the œsophageal ring having been situated in the region of the fourth ventricle, a continuation of the spinal canal could not be present in front of this part. If, on the other hand, the cerebro-spinal canal appeared after the disappearance of the primitive mouth, its roof must necessarily also be a formation subsequent to the atrophy of the mouth, and varieties of structure in it can have no bearing upon the previous position of the mouth.

But apart from speculations upon the origin of the spinal cord, there are strong arguments against Dr Dohrn's view about the fourth ventricle. In the first place, were the fourth ventricle to be the part of the nervous system which previously formed the œsophageal commissures, we should expect to find the opening in the nervous system at this point to be visible at an early period of development, and at a later period to cease to be so. The reverse is however the case. In early embryonic life the roof of the fourth ventricle is indistinguishable from other parts of the nervous system, and only thins out at a later period. Further than this, any explanation of the thin roof of the fourth ventricle ought also to elucidate

the nearly similar structure in the sinus rhomboidalis, and cannot be considered satisfactory unless it does so.

The peculiarities of the cerebro-spinal canal in the region of the brain appear to me to present considerable difficulties in the way of comparing the central nervous system of Vertebrates and segmented Annelids. The manner in which the cerebro-spinal canal is prolonged into the optic vesicles, the cerebral and the optic lobes is certainly opposed both to an intelligible explanation of the spinal canal itself, and also to a comparison of the two nervous systems under consideration.

Its continuation into the cerebral hemispheres and into the optic lobes (mid-brain) may perhaps be looked upon as due to peculiar secondary growths of those two ganglia, but it is very difficult to understand its continuation into the optic vesicles.

If it be granted that the spinal canal has arisen from a folding in of the external skin, then the present inner surface of the optic vesicle must also have been its original outer surface, and it follows as a necessary consequence that the present position of the rods and cones behind and not in front of the nervous structures of the retina was not the primitive one. The rods and cones arise, as is well known, from the inner surface of the outer portion of the optic vesicle, and must, according to the above view, be supposed originally to have been situated on the external surface, and have only come to occupy their present position during the folding in, which resulted in the spinal canal. On *à priori* grounds we should certainly expect the rods and cones to have resulted from the differentiation of a layer of cells external to the conducting nervous structures. The position of the rods and cones posterior to these suggests therefore that some peculiar infolding has occurred, and may be used as an argument to prove that the medullary groove is no mere embryonic structure, but the embryonic repetition of an ancestral change. The supposition of such a change of position in the rods and cones necessarily implies that the folding in to form the spinal canal must have been a very slow one. It must have given time to the refracting media of the eye gradually to travel round, so as still to maintain their primitive position, while in successive generations a rudimentary spinal

furrow carrying with it the retina became gradually converted into a canal[1].

If Dr Dohrn's comparison of the vertebrate nervous system with that of segmented Annelids be accepted, the following two points must in my opinion be admitted:—

(1) That the formation of the cerebro-spinal canal was subsequent to the loss of the old mouth.

(2) That the position of the old mouth is still unknown.

The well-known view of looking at the pituitary and pineal growths as the remnants of the primitive œsophagus, has no doubt some features to recommend it. Nearly conclusive against it is the fact that the pituitary involution is not, as used to be supposed, a growth towards the infundibulum of the hypoblast of the œsophagus, but of the epiblast of the mouth. It is almost inconceivable that an involution from the present mouth can have assisted in forming part of the old œsophagus.

There is a view not involving the difficulty of the œsophageal ring, fresh mouth[2], and of the change of the ventral to

[1] Professor Huxley informs me that he has for many years entertained somewhat similar views to those in the text about the position of the rods and cones, and has been accustomed to teach them in his lectures.

[2] Professor Semper (*Die Verwandtschaftsbeziehungen d. gegliederten Thiere, Arbeiten aus d. Zool.-zoot. Institut*, Würzburg, 1876) has some interesting speculations on the difficult question of the vertebrate mouth, which have unfortunately come to my knowledge too late to be either fully discussed or incorporated in the text. These speculations are founded on a comparison of the condition of the mouth in Turbellarians and Nemertines. He comes to the conclusion that there was a primitive mouth on the cardiac side of the supra-œsophageal ganglion, which is the existing mouth of Turbellarians and Vertebrates and the opening of the proboscis of Nemertines, but which has been replaced by a fresh mouth on the neural side in Annelids and Nemertines. In Nemertines however the two mouths co exist—the vertebrate mouth as the opening of the proboscis, and the Annelid mouth as the opening for the alimentary tract. This ingenious hypothesis is supported by certain anatomical facts, which do not appear to me of great weight, but for which the reader must refer to the original paper. It no doubt avoids the difficulty of the present position of the vertebrate mouth, but unfortunately at the same time substitutes an equal difficulty in the origin of the Annelidan mouth. This Professor Semper attempts to get over by an hypothesis which to my mind is not very satisfactory (p. 378), which, however, and this Professor Semper does not appear to have noticed, *could equally well be employed to explain the origin of a Vertebrate mouth as a secondary formation subsequent to the Annelidan mouth.* Under these circumstances this fresh hypothesis does not bring us very much nearer to a solution of the vertebrate-annelid mouth question, but merely substitutes one difficulty for another; and does not appear to me so satisfactory as the hypothesis suggested in the text.

At the same time Professor Semper's hypothesis suggests an explanation of that curious organ the Nemertine proboscis. If the order of changes

the dorsal surface, which, though so far unsupported by any firm basis of observed facts, nevertheless appears to me worth suggesting. It assumes that Vertebrates are descended *not* through the present line of segmented Vermes, but through some other line which has now, so far as is known, completely vanished. This line must be supposed to have originated from the same *unsegmented Vermes* as the present segmented Annelids. They therefore acquired fundamentally similar segmental and other Annelidan organs.

The difference between the two branches of the Vermes lay in the nervous system. The unsegmented ancestors of the *present* Annelids seem to have had a pair of super-œsophageal ganglia, from which two main nervous stems extended backwards, one on each side of the body. Such a nervous system in fact as is possessed by existing Nemertines or Turbellarians[1]. As the Vermes became segmented and formed the Annelids, these side nerves seem to have developed ganglia, corresponding in number with the segments, and finally, approximating on the ventral surface, to have formed the ventral cord[2].

The other branch of Vermes which I suppose to have been the ancestors of Vertebrates started from the same stock as existing Annelids, but I conceive the lateral nerve-cords, instead of approximating ventrally, to have done so dorsally, and thus a dorsal cord to have become formed analogous to the ventral cord of living Annelids, only without an œsophageal nerve-ring[3].

It appears to me, (if the difficulties of comparing the Annelidan ventral cord with the spinal cord of Vertebrates are found to be insurmountable), that this hypothesis would involve far fewer improbabilities than one which supposes the whole central nervous system of Vertebrates to be homologous with

suggested by him were altered it might be possible to suppose that there never was more than one mouth for all Vermes, but that the proboscis in Nemertines gradually split itself off from the œsophagus to which it originally belonged, and became quite free and provided with a separate opening and perhaps carried with it the so-called vagus of Professors Semper and Leydig.

[1] It is not of course to be supposed that the primitive nervous system was pierced by a proboscis like that of the Nemertines.

[2] This is Gegenbaur's view of the development of the ventral cord, and I regard it in the meantime as the most probable view which has been suggested.

[3] A dorsal instead of a ventral approximation of the lateral nerve-cords would be possible in the descendants of such living segmented Vermes as Saccocirrus and Polygordius.

the super-œsophageal ganglia. The mode of formation of a nervous system presupposed in my hypothesis, well accords with what we know of the formation of the ventral cord in existing Annelids.

The supposition of the existence of another branch of segmented Vermes is not a very great difficulty. Even at the present day we have possibly more than one branch of Vermes which have independently acquired segmentation, viz.: the Chœtopodous Annelids and the Hirudinea. If the latter is an isolated branch, it is especially interesting from having independently developed a series of segmental organs like those of Chœtopodous Annelids, which we must suppose the ancestors of Vertebrates also to have done if they too form an independent branch.

In addition to the difficulty of imagining a fresh line of segmented Vermes, there is another difficulty to my view, viz.: the fact that in almost all Vermes, the blood flows forwards in the dorsal vessel, and backwards in the ventral vessel. This condition of the circulation very well suits the view of a change of the dorsal for the ventral surfaces, but is opposed to these surfaces being the same for Vertebrates and Vermes. I cannot however regard this point as a very serious difficulty to my view, considering how undefined is the circulation in the unsegmented groups of the Vermes.

Sympathetic nervous system.—Between stages K and L there may be seen short branches from the spinal nerves, which take a course towards the median line of the body, and terminate in small irregular cellular masses immediately dorsal to the cardinal veins. These form the first traces that have come under my notice of the sympathetic nervous system. In the youngest of my embryos in which I have detected these it has not been possible for me either definitely to determine the antero-posterior limits of the system, or to make certain whether the terminal masses of cells which form the ganglia are connected by a longitudinal commissure. In a stage slightly younger than L the ganglia are much more definite, the anterior one is situated in the cardiac region close to the end of the intestinal branch of the vagus, and the last of them quite at the posterior

end of the abdominal cavity. The anterior ganglia are the largest; the commissural cord, if developed, is still very indistinct. In stage L the commissural cord becomes quite definite, and the ganglia become so considerable as not to be easily overlooked. They are represented in Pl. XV. fig. 1, *sy. g.* in the normal position immediately above the cardinal veins. The branches connecting them with the trunks of the spinal nerves may still be seen without much difficulty. In later stages these branches cannot easily be made out in sections, but the ganglia themselves continue as fairly conspicuous objects.

The sympathetic system only came under my notice at a comparatively late period in my investigations, and the above facts do not in all points clear up its development. My observations seem to point to the sympathetic system arising as an off-shoot from the cerebrospinal system. Intestinal branches would seem to be developed on the main nerve stems of this in the thoracic and abdominal regions, each of these then developes a ganglion, and the ganglia become connected by a longitudinal commissure. On this view a typical spinal nerve has the following parts: two roots, a dorsal and ventral, the dorsal one ganglionated, and three main branches, (1) a ramus dorsalis, (2) a ramus ventralis, and (3) a ramus intestinalis. This scheme may be advantageously compared with that of a typical cranial nerve according to Gegenbaur. It may be noted that it brings the sympathetic nervous system into accord with the other parts of the nervous system as a product of the epiblast, and derived from outgrowths from the neural axis. It is clear, however, that my investigations, though they may naturally be interpreted in this way, do not definitely exclude a completely different method of development for the sympathetic system.

THE DEVELOPMENT OF THE BRAIN.

General History. In stage G the brain presents a very simple constitution (Vol. x. Pl. XXIV. fig. G), and is in fact little more than a dilated termination to the cerebro-spinal axis. Its length is nearly one-third that of the whole body, being proportionately very much greater than in the adult.

It is divided by very slight constrictions into three lobes, the posterior of which is considerably the largest. These are known as the fore-brain, the mid-brain, and the hind-brain. The anterior part of the brain is bent slightly downwards about an axis passing through the mid-brain. The walls of the brain, composed of several rows of elongated columnar cells, have a fairly uniform thickness, and even the roof of the hind-brain is as thick as any other part. Towards the end of stage G the section of the hind-brain becomes somewhat triangular with the apex of the triangle directed downwards.

In Pristiurus during stage H no very important changes take place in the constitution of the brain. In Scyllium, however, indications appear in the hind-brain of its future division into a cerebellum and medulla oblongata. The cavity of the anterior part dilates and becomes rounded, while that of the posterior part assumes in section an hour-glass shape, owing to an increase in the thickness of the lateral parts of the walls. At the same time the place of the original thick roof is taken by a very thin layer, which is formed not so much through a change in the character and arrangements of the cells composing the roof, as by a divarication of the two sides of the hind-brain, and the simultaneous introduction of a fresh structure in the form of a thin sheet of cells connecting dorsally the diverging lateral halves of this part of the brain. By stage I, the hind-brain in Pristiurus also acquires an

hour-glass shaped section, but the roof has hardly begun to thin out (Pl. XVII. fig. 4a and 4b).

During stages I and K the cranial flexure becomes more and more pronounced, and causes the mid-brain definitely to form the termination of the long axis of the embryo (Pl. XVII. fig. 1, 2, etc.), and before the close of stage K a thin coating of white matter has appeared on the exterior of the whole brain, but no other histological changes of interest have occurred.

During stage L an apparent rectification of the cranial flexure commences, and is completed by stage Q. The changes involved in this process may be advantageously studied by comparing the longitudinal sections of the brain during stages L, P, and Q, represented in Pl. XVIII. fig. 1*a*, 5 and 7*a*.

It will be seen, first of all, that so far from the flexure of the brain itself being diminished, it is increased, and in P (fig. 5) the angle in the floor of the mid-brain becomes very acute indeed; in other words, the anterior part of the brain has been bent upon the posterior through nearly two right angles, and the infundibulum, or primitive front end of the brain, now points nearly directly backwards. At the same time the cerebral hemispheres have grown directly forwards, and if figures 1*a* and 5 in Plate XVIII. be compared it will be seen that in the older brain of the two the cerebral hemispheres have assumed a position which might be looked on as the result of their having been pushed dorsalwards and forwards against the mid-brain, and having in the process pressed in and nearly obliterated the original thalamencephalon. The thalamencephalon in fig. 1*a*, belonging to stage L, is relatively large, but in fig. 5, belonging to stage P, it only occupies a very small space between the front wall of the mid-brain and the hind wall of the cerebral hemispheres. It is therefore in part by the change in position of the cerebral hemispheres that the angle between the trabeculæ and parachordals becomes increased, *i.e.* their flexure *diminished*, while at the same time the flexure of the brain itself is *increased*. More important perhaps in the apparent rectification of the cranial flexure than any of the previously mentioned points, is the appearance of a bend in the hind-brain which tends to correct the original cranial flexure. The gradual growth of this fresh flexure can be studied in the longitudinal sections

which have been represented. It is at its maximum in stage Q. This short preliminary sketch of the development of the brain as a whole will serve as an introduction to the history of the individual divisions of the brain.

Fore-brain. In its earliest condition the fore-brain forms a single vesicle without a trace of separate divisions, but buds off very early the optic vesicles, whose history is described with that of the eye (Pl. XVII. fig. 3, *op. v*). Between stages I and K the posterior part of the fore-brain sends outwards a papilliform process towards the exterior, which forms the rudiment of the pineal gland (Pl. XVII. fig. 1, *pn*). Immediately in front of the rudiment a constriction appears, causing a division of the fore-brain into a large anterior and a small posterior portion. This constriction is shallow at first, but towards the close of stage K becomes much deeper (Pl. XVII. fig. 2 and fig. 16*a*), leaving however the two cavities of the two divisions of the fore-brain united ventrally by a somewhat wide canal.

The posterior of the two divisions of the fore-brain forms the thalamencephalon. Its anterior wall adjoining the cerebral rudiment becomes excessively thin (Pl. XVII. fig. 11); and its base till the close of stage K is in close contact with the mouth involution, and presents but a very inconspicuous prominence which marks the eventual position of the infundibulum (Pl. XVII. fig. 9*a*, 12, 16, *in*). The anterior and larger division of the fore-brain forms the rudiment of the cerebral hemispheres and olfactory lobes. Up to stage K this rudiment remains perfectly simple, and exhibits no signs, either externally or internally, of a longitudinal constriction into two lobes. From the canal uniting the two divisions of the fore-brain (which eventually forms part of the thalamencephalon) there spring the hollow optic nerves. A slight ventral constriction separating the cerebral rudiment from that part of the brain where these are attached appears even before the close of stage K (Pl. XVII. fig. 11, *op.n*).

During stage L the infundibulum becomes much produced, and forms a wide sack in contact with the pituitary body, and its cavity communicates with that of the third ventricle by an elongated slit-like aperture. This may be seen by comparing Pl. XVIII. fig. 1*a* and 1*c*. In fig. 1*c* taken along the middle line,

there is present a long opening into the infundibulum (*in*), which is shown to be very narrow by being no longer present in fig. 1*a* representing a section slightly to one side of the middle line. During the same stage the pineal gland grows into a sack-like body, springing from the roof of the thalamencephalon, fig. 1*b*, *pn*. This latter (the thalamencephalon) is now dorsally separated from the cerebral rudiment by a deep constriction, and also ventrally by a less well marked constriction. At its side also a deep constriction is being formed in it, immediately behind the pineal gland. The cerebral rudiment is still quite unpaired and exhibits no sign of becoming constricted into two lobes.

During the next two stages the changes in the fore-brain are of no great importance, and I pass at once to stage O. The infundibulum is now nearly in the same condition as during stage L, though (as is well shown in the figure of a longitudinal section of the next stage) it points more directly backwards than before. The remaining parts of the thalamencephalon have however undergone considerable changes. The more important of these are illustrated by a section of stage O, Pl. XVIII. fig. 3, transverse to the long axis of the embryo, and therefore, owing to the cranial flexure, cutting the thalamencephalon longitudinally and horizontally; and for stage P in a longitudinal and vertical section through the brain (Pl. XVIII. fig. 5). In the first place the roof of the thalamencephalon has become very much shortened by the approximation of the cerebral rudiment to the mid-brain. The pineal sack has also become greatly elongated, and its somewhat dilated extremity is situated between the cerebral rudiment and the external skin. It opens into the hind end of the third ventricle, and its posterior wall is continuous with the front wall of the mid-brain. The sides of the thalamencephalon have become much thickened, and form distinct optic thalami (*op.*) united by a very well marked posterior commissure (*p c.*). The anterior wall of the thalamencephalon as well as its roof are very thin. The optic nerves have become by stage O quite solid except at their roots, into which the ventricles of the fore-brain are for a short distance prolonged. This solidification is arrived at, so far as I have determined, without the intervention of a fold. The

nerves are fibrous, and a commencement of the chiasma is certainly present. From the chiasma there appears to pass out on each side a band of fibres, which runs near the outer surface of the brain to the base of the optic lobes (mid-brain), and here the fibres of the two sides again cross.

By stage O important changes are perceptible in the cerebral rudiment. In the first place there has appeared a slight fold at its anterior extremity (Pl. XVIII. fig. 3, *x*), destined to form a vertical septum dividing it into two hemispheres, and secondly, lateral outgrowths (vide Pl. XVIII. fig. 2, *ol.l*), to form the olfactory lobes. Its thin posterior wall presents on each side a fold which projects into the central cavity. From the peripheral end of each olfactory lobe a nerve similar in its histological constitution to any other cranial nerve makes its appearance (Pl. XVIII. fig. 2); this divides into a number of branches, one of which passes into the connective tissue between the two layers of epithelium in each Schneiderian fold. On the root of this nerve there is a large development of ganglionic cells. I have not definitely observed its origin, but have no reason to doubt that it is a direct outgrowth from the olfactory lobe, exactly similar *in its mode of development* to any other nerve of the body.

The cerebral rudiment undergoes great changes during stage P. In addition to a great increase in the thickness of its walls, the fold which appeared in the last stage has grown backwards, and now divides it in front into two lobes, the rudiments of the cerebral hemispheres. The greater and posterior section is still however quite undivided, and the cavities of the lobes (lateral ventricles) though separated in front are still quite continuous behind. At the same time, the olfactory lobes, each containing a prolongation of the ventricle, have become much more pronounced (vide fig. 4*a* and 4*c*, *ol.l*). The root of the olfactory nerve is now very thick, and the ganglion cells it contains are directly prolonged into the ganglionic portion of the olfactory bulb; in consequence of which it becomes rather difficult to fix on the exact line of demarcation between the bulb and the nerve.

Stage Q is the latest period in which I have investigated the development of the brain. Its structure is represented for

this stage in general view in Pl. XVIII. fig. 6a, 6b, 6c, in longitudinal section in Pl. XVIII. fig. 7a, 7b, and in transverse section Pl. XVIII. fig. 8a—d. The transverse sections are taken from a somewhat older embryo than the longitudinal. In the thalamencephalon there is no fresh point of great importance to be noticed. The pineal gland remains as before, and has become, if anything, longer than it was, and extends further forwards over the summit of the cerebrum. It is situated, as might be expected, in the connective tissue within the cranial cavity (fig. 8a, *pn*), and does not extend outside the skull, as it appears to do, according to Götte's investigations, in Amphibians. Götte[1] compares the pineal gland with the long persisting pore which leads into the cavity of the brain in the embryo of Amphioxus, and we might add the Ascidians, and calls it "ein Umbildungsprodukt einer letzten Verbindung des Hirns mit der Oberhaut." This suggestion appears to me a very good one, though no facts have come under my notice which confirm it. The sacci vasculosi are perhaps indicated at this stage in the two lateral divisions of the trilobed ventricle of the infundibulum (fig. 8c).

The lateral ventricles (fig. 8a) are now quite separated by a median partition, and a slight external constriction marks the lobes of the two hemispheres; these, however, are still united by nervous structures for the greater part of their extent. The olfactory lobes are formed of a distinct bulb and stalk (fig. 8a, *ol.l*), and contain, as before, prolongations of the lateral ventricles. The so-called optic chiasma is very distinct (fig. 8b, *op.n*), but the fibres from the optic nerves appear to me simply to cross and not to intermingle.

The mid-brain. The mid-brain is at first fairly marked off from both the fore and hind brains, but less conspicuously from the latter than from the former. Its roof becomes progressively thinner and its sides thicker up to stage P, its cavity remaining quite simple. The thinness of the roof gives it, in isolated brains of stage P, a bilobed appearance, (vide Pl. XVIII. fig. 4b, *mb*, in which the distinctness of this character is by no means exaggerated). During stage Q it becomes really bilobed through the formation in its roof of a shallow median furrow,

[1] *Ent. d. Unke*, p. 304.

(Pl. XVIII. fig. 8*b*). Its cavity exhibits at the same time the indication of a division into a central and two lateral parts.

The hind-brain. The hind-brain has at first a fairly uniform structure, but by the close of stage I, the anterior part becomes distinguished from the remainder by the fact, that its roof does not become thin as does that of the posterior part. This anterior, and *at first very insignificant portion*, forms the rudiment of the cerebellum. Its cavity is quite simple and is continued uninterruptedly into that of the remainder of the hind-brain. The cerebellum assumes in the course of development a greater and greater prominence, and eventually at the close of stage Q overlaps both the optic lobes in front and the medulla behind (Pl. XVIII. fig. 7*a*). It exhibits in surface-views of the hardened brain of stages P and Q the appearance of a median constriction, and the portion of the ventricle contained in it is prolonged into two lateral outgrowths (Pl. XVIII. fig. 8*c* and 8*d*, *cb*).

The posterior section of the hind-brain which forms the medulla undergoes changes of a somewhat complicated character. In the first place its roof becomes in front very much extended and thinned out. At the raphe, where the two lateral halves of the brain originally united, a separation, as it were, takes place, and the two sides of the brain become pushed apart, remaining united by only a very thin layer of nervous matter (Pl. XVII. fig. 6, iv. v.). As a result of this peculiar growth in the brain, the roots of the nerves of the two sides which were originally in contact at the dorsal summit of the brain become carried away from one another, and appear to arise at the sides of the brain (Pl. XVII. fig. 6 and 7). Other changes also take place in the walls of the brain. Each lateral wall presents two projections towards the interior (Pl. XVII. fig. 5*a*). The ventral of these vanish, and the dorsal approximate so as nearly to divide the cavity of the hind-brain, or fourth ventricle, into a large dorsal and a small ventral channel (Pl. XVII. fig. 6), and this latter becomes completely obliterated in the later stages. The dorsal pair, while approximating, also become more prominent, and stretch into the dorsal moiety of the fourth ventricle (Pl. XVII. fig. 6). They are still very prominent at stage Q (Pl. XVIII. fig. 8*d*, *f t*), and correspond in position with the fasciculi

teretes of human anatomy. Part of the root of the seventh nerve originates from them. They project freely in front into the cavity of the fourth ventricle (Pl. XVIII. fig. 7).

By stage Q restiform tracts are indistinctly marked off from the remainder of the brain, and are anteriorly continued into the cerebellum. Near their junction with the cerebellum they form prominent bodies (Pl. XVIII. fig. 7*a*, *r t*), which are regarded by Miklucho-Maclay[1] as representing the true cerebellum.

By stage O the medulla presents posteriorly, projecting into its cavity, a series of lobes which correspond with the main roots (not the branches) of the vagus and glosso-pharyngeal nerves (Pl. XIX. fig. 5). There appear to me to be present seven or eight projections: their number cannot however be quite certainly determined. The first of them belongs to the root of the glosso-pharyngeal, the next one is interposed between the glosso-pharyngeal and the first root of the vagus, and is without any corresponding nerve-root. The next five correspond to the five main roots of the vagus. For each projection to which a nerve pertains there is a special nucleus of nervous matter, from which the root springs. These nuclei do not stain like the remainder of the walls of the medulla, and stand out accordingly very conspicuously in stained sections.

The coating of white matter which appeared at the end of stage K, on the exterior of each lateral half of the hind-brain, extends from a point just dorsal to the attachment of the nerve-roots to the ventral edge of the medulla, and is specially connected with the tissue of the upper of the two already described projections into the fourth ventricle.

A rudiment of the tela vasculosa makes its appearance during stage Q, and is represented by the folds in the wall of the fourth ventricle in my figure of that stage (Pl. XVIII. fig. 7*a*, *t v*).

The development of the brain in Elasmobranchs has already been worked out by Professor Huxley, and a brief but in many respects very complete account of it is given in his recent paper on Ceratodus[2]. He says, pp. 30 and 31, "The development of the cerebral hemispheres in Plagiostome Fishes

[1] *Das Gehirn d. Selachier*, Leipzig, 1870.
[2] *Proceedings of the Zoological Society*, 1876, Pt. I. p. 30 and 31.

differs from the process by which they arise in the higher Vertebrata. In a very early stage, when the first and second visceral clefts of the embryo Scyllium are provided with only a few short branchial filaments, the anterior cerebral vesicle is already distinctly divided into the thalamencephalon (from which the large infundibulum proceeds below, and the small tubular peduncle of the pineal gland above, while the optic nerve leaves its sides) and a large single oval vesicle of the hemispheres. On the ventral face of the integument covering these are two oval depressions, the rudimentary olfactory sacs.

"As development proceeds the vesicle of the hemispheres becomes divided by the ingrowth of a median longitudinal septum, and the olfactory lobes grow out from the posterior lateral regions of each ventricle thus formed, and eventually rise on to the dorsal faces of the hemispheres, instead of, as in most Vertebrata, remaining on their ventral sides. I may remark, that I cannot accept the views of Miklucho-Maclay, whose proposal to alter the nomenclature of the parts of the Elasmobranch's brain, appears to me to be based upon a misinterpretation of the facts of development."

The last sentence of the paragraph brings me to the one part on which it is necessary to say a few words, viz. the views of Miklucho-Maclay. His views have not received any general acceptance, but the facts narrated in the preceding section show, beyond a doubt, that he has 'misinterpreted' the facts of development, and that the ordinary view of the homology of the parts is the correct one. A comparison of the figures I have given of the embryo brain with similar figures of the brain of higher Vertebrates shows this point conclusively. Amongst the features of the embryonic brain of Elasmobranchs, the long persisting unpaired condition of the cerebral hemisphere, upon which so much stress has already been laid by Professor Huxley, appears to me to be one of great importance, and may not improbably be regarded as a real ancestral feature. Some observations have recently been published by Professor B. G. Wilder[1] upon this point, and upon the homologies and development of the olfactory lobes. Fairly good figures are given to illustrate

[1] Anterior brain-mass with Sharks and Skates, *American Journal of Science and Arts*, Vol. XII. 1876.

the development of the cerebral hemispheres, but the conclusions arrived at aré in part opposed to my own results. Professor Wilder says: "The true hemispheres are the lateral masses, more or less completely fused in the middle line, and sometimes developing at the plane of union a bundle of longitudinal commissural fibres. The hemispheres retain their typical condition as anterior protrusions of the anterior vesicle; but they lie mesiad of the olfactory lobes, *and in Mustelus at least seem to be formed after them.*" The italics are my own. From what has been said above, it is clear that the statement italicised, for Scyllium at least, completely reverses the order of development. Still more divergent from my conclusions are Professor Wilder's statements on the olfactory lobes. He says: "The true olfactory lobe, or rhinencephalon, seems, therefore, to embrace only the hollow base of the crus, more or less thickened, and more or less distinguishable from the main mass as a hollow process. The olfactory bulb, with the more or less elongated crus of many Plagiostomes, seems to be developed independently, or in connection with the olfactory sack, as are the general nerves;" and again, "But the young and adult brains since examined show that the ventricle (*i.e.* the ventricle of the olfactory lobe) ends as a rounded cul-de-sac before reaching the 'lobe'."

The majority of the statements contained in the above quotations are not borne out by my observations. Even the few preparations of which I have given figures, appear to me to prove that (1) the olfactory lobes (crura and bulbs) are direct outgrowths from the cerebral rudiment, and develope quite independently of the olfactory sack; (2) that the ventricle of the cerebral rudiment does not stop short at the base of the crus; (3) that from the bulb a nerve grows out which has a centrifugal growth like other nerves of the body, and places the central olfactory lobe in communication with the peripheral olfactory sack. In some other Vertebrates this nerve seems hardly to be developed, but it is easily intelligible, that if in the ordinary course of growth the olfactory sack became approximated to the olfactory lobe, the nerve which grew out from the latter to the sack might become so short as to escape detection.

Organs of Sense.

The olfactory organ. The olfactory pit is the latest formed of the three organs of special sense. It appears during a stage intermediate between *I* and *K*, as a pair of slight thickenings of the external epiblast, in the normal vertebrate position on the under side of the fore-brain immediately in front of the mouth (Pl. XVII. fig. 1 and 2, *ol*).

The epiblast cells which form this thickening are very columnar, but present no special peculiarities. Each thickened patch of skin soon becomes involuted as a shallow pit, which remains in this condition till the close of the stage *K*. The epithelium very early becomes raised into a series of folds (Schneiderian folds). These are bilaterally symmetrical, and diverge like the barbs of a feather from a median line (Pl. XVII. fig. 14). The nasal pits at the close of stage K are still separated by a considerable interval from the walls of the brain, and no rudiment of an olfactory lobe arises till a later period; but a description of the development of this as an integral part of the brain has already been given, p. 444.

Eye. The eye does not present in its early development any very special features of interest. The optic vesicles arise as hollow outgrowths from the base of the fore-brain (Pl. XVII. fig. 3, *op.v*), from which they soon become partially constricted, and form vesicles united to the base of the brain by comparatively narrow hollow stalks, the rudiments of the optic nerves. The constriction to which the stalk or optic nerve is due takes place from above and backwards, so that the optic nerves open into the base of the front part of the thalamencephalon (Pl. XVII. fig. 13*a*, *op n*). After the establishment of the optic nerves, there take place the formation of the lens and the pushing in of the anterior wall of the optic vesicle towards the posterior.

The lens arises in the usual vertebrate fashion. The epiblast in front of the optic vesicle becomes very much thickened, and then involuted as a shallow pit, which eventually deepens and narrows. The walls of the pit are soon constricted off as a nearly spherical mass of cells enclosing a very small central cavity, in some cases indeed so small as to be barely recognisable (Pl. XVII. fig. 7, *l*). The pushing in of the anterior wall

of the optic vesicle towards the posterior takes place in quite the normal manner; but, as has been already noticed by Götte[1] and others, is not a simple mechanical result of the formation of the lens, as is shown by the fact that the vesicle assumes a flattened form even before the appearance of the lens. The whole exterior of the optic cup becomes invested by mesoblast, but *no mesoblastic cells grow in between the lens and the adjoining wall of the optic cup.*

Round the exterior of the lens, and around the exterior and interior of the optic cup, there appear membrane-like structures, similar to those already described round the spinal cord and other organs. These membrane-like structures appear with a varying distinctness, but at the close of stage *K* stand out with such remarkable clearness as to leave no doubt that they are not artificial products (Pl. XVII. fig. 13*a*). They form the rudiments of the hyaloid membrane and lens capsule. Similar, though less well marked membranes, may often be seen lining the central cavity of the lens and the space between the two walls of the optic cup. The optic cup is at first very shallow, but owing to the rapid growth of the free edge of its walls soon becomes fairly deep. The growth extends to the whole circumference of the walls except the point of entrance of the optic nerve (Pl. XVII. fig. 13*a*), where no growth takes place; here accordingly a gap is left in the walls, which forms the well known choroid slit. While this double walled cup is increasing in size, the wall lining the cavity of the cup becomes thick, and the outer wall very thin (fig. 13*a*). No further differentiations arise before the close of stage K.

The lens is carried outwards with the growth of the optic cup, leaving the cavity of the cup quite empty. It also grows in size, and its central cavity becomes larger. Still later its anterior wall becomes very thin, and its posterior wall thick, and doubly convex (fig. 13*a*). Its changes, however, so exactly correspond to those already known in other Vertebrates, that a detailed description of them would be superfluous. *No mesoblast passes into the optic cup round its edge,* but a process of mesoblast, accompanied by a blood-vessel, passes into the space between the lens and the wall of the optic cup through

[1] *Entwickelungsgeschichte d. Unke.*

the choroid slit (fig. 13*a*, *ch*). This process of tissue is very easily seen, and swells out on entering the optic cup into a mushroom-like expansion. It forms the processus falciformis, and from it is derived the vitreous humour.

About the development of the parts of the eye, subsequently to stage *K*, I shall not say much. The iris appears during stage *O*, as an ingrowing fold of both layers of the optic cup with a layer of mesoblast on its outer surface, which tends to close over the front of the lens. Both the epiblast layers comprising the iris are somewhat atrophied, and the outer one is strongly pigmented. At stage O the mesoblast first also grows in between the external skin and the lens to form the rudiment of the mesoblastic structures of the eye in front of the lens. The layer, when first formed, is of a great tenuity.

The points in my observations, to which I attach the greatest importance, are the formation of the lens capsule and the hyaloid membrane; with the development of these may be treated also that of the vitreous humour and rudimentary *processus falciformis*. The development of these parts in Elasmobranchs has recently been dealt with by Dr Bergmeister[1], and his observations with reference to the vitreous humour and processus falciformis, the discovery of which in embryo Elasmobranchs is due to him, are very complete. I cannot, however, accept his view that the hyaloid membrane is a mesoblastic product. Through the choroid slit there grows, as has been said, a process of mesoblast, the processus falciformis, which on entering the optic cup dilates, and therefore appears mushroom-shaped in section. At the earliest stage (K) a blood-vessel appeared in connection with it, but no vascular structure came under my notice in the later stages. The structure of this process during stage P is shown in Pl. XIX. fig. 6, *p. fal.*; it is there seen to be composed of mesoblast-cells with fibrous prolongations. The cells, as has been noticed by Bergmeister, form a special border round its dilated extremity. This process is formed much earlier than the vitreous humour, which is first seen in stage O. In hardened specimens this latter appears either as a gelatinous mass with a meshwork of fibres

[1] *Embryologie d. Coloboms, Sitz. d. k. Akad. Wien*, Bd. LXXI. 1875.

or (as shown in Pl. XIX. fig. 6) with elongated fibres proceeding from the end of the processus falciformis. These fibres are probably a product of the hardening reagent, but perhaps represent some preformed structure in the vitreous humour. I have failed to detect in it any cellular elements. It is more or less firmly attached to the hyaloid membrane.

On each side of the processus falciformis in stage P a slight fold of the optic cup is to be seen, but folds so large as those represented by Bergmeister have never come under my notice, though this may be due to my not having cut sections of such late embryos as he has. The hyaloid membrane appears long before the vitreous humour as a delicate basement membrane round the inner surface of the optic cup (Pl. XVII. fig. 13*a*), which is perfectly continuous with a similar membrane round the outer surface. In the course of development the hyaloid membrane becomes thicker than the membrane outside the optic cup, with which however it remains continuous. This is very clear in my sections of stage M. By stage O the membrane outside the cup has ceased to be distinguishable, but the hyaloid membrane may nevertheless be traced to the very edge of the cup round the developing iris; but does not unite with the lens capsule. It can also be traced quite to the junction of the two layers of the optic cup at the side of the choroid slit (Pl. XIX. fig. 6, *hy. m*). When the vitreous humour becomes artificially separated from the retina, the hyaloid membrane sometimes remains attached to the former, but at other times retains in preference its attachment to the retina. My observations do not throw any light upon the junction of the hyaloid membrane and lens capsule to form the suspensory ligament, nor have I ever seen (as described by Bergmeister) the hyaloid membrane extending across the free end of the processus falciformis and separating the latter from the vitreous humour. This however probably appears at a period subsequent to the latest one investigated by me. The lens capsule arises at about the same period as the hyaloid membrane, and is a product of the cells of the lens. It can be very distinctly seen in all the stages subsequent to its first formation. The proof of its being a product of the epiblastic lens, and not of the mesoblast, lies mainly in the fact of there being no mesoblast

at hand to give rise to it at the time of its formation, vide Pl. XVII, fig. 13 *a*. If the above observations are correct, it is clear that the hyaloid membrane and lens capsule are respectively products of the retina and lens; so that it becomes necessary to go back to the older views of Kölliker and others in preference to the more modern ones of Lieberkühn and Arnold. It would take me too far from my subject to discuss the arguments used by the later investigators to maintain their view that the hyaloid membrane and lens capsule are mesoblastic products; but it will suffice to say that the continuity of the hyaloid membrane over the pecten in birds is no conclusive argument against its retinal origin, considering the great amount of apparently independent growth which membranes, when once formed, are capable of exhibiting.

Bergmeister's and my own observations on the vitreous humour clearly prove that this is derived from an ingrowth through the choroid-slit. On the other hand, the researches of Lieberkühn and Arnold on the Mammalian Eye appear to demonstrate that a layer of mesoblast becomes in Mammalia involuted with the lens, and that from this the vitreous humour (including the *membrana capsulo-pupillaris*) is said to be formed. Lieberkühn states that in Birds the vitreous humour is formed in a similar fashion. I cannot, however, accept his results on this point. It appears, therefore, that, so far as is known, all groups of Vertebrata, with the exception of Mammalia, conform to the Elasmobranch type. The differences between the types of Mammalia and remaining Vertebrata are, however, not so great as might at first sight appear. They are merely dependent on slight differences in the manner in which the mesoblast enters the optic cup. In the one case it grows in round one specialized part of the edge of the cup, *i.e.* the choroid-slit; in the other, round the whole edge, including the choroid-slit. Perhaps the mode of formation of the vitreous humour in Mammalia may be correlated with the early closing of the choroid-slit.

Auditory Organ. With reference to the development of the organ of hearing I have very little to say. Opposite the interval between the seventh and the glosso-pharyngeal nerves the

external epiblast becomes thickened, and eventually involuted as a vesicle which remains however in communication with the exterior by a narrow duct. Towards the close of stage K the auditory sack presents three protuberances—one pointing forwards, a second backwards, and a third outwards. These are respectively the rudiments of the anterior and posterior vertical and external horizontal semicircular canals. These rudiments are easily visible from the exterior (Pl. XVII, fig. 2).

As has been already pointed out, the epiblast of Elasmobranchs during the early periods of development exhibits no division into an epidermic and a nervous layer, and in accordance with its primitive undifferentiated condition, those portions of the organs of sense which are at this time directly derived from the external integument are formed indiscriminately from the whole, and not from an inner or so-called nervous part of it only. In the Amphibians the auditory sack and lens are derived from the nervous division of the epiblast only, while the same division of the layer plays the major part in forming the olfactory organ. It is also stated that in Birds and Mammals the part of the epiblast corresponding to the nervous layer is alone concerned in the formation of the lens, though this does not appear to be the case with the olfactory or auditory organs in these groups.

Mouth involution and Pituitary body.

The development of the mouth involution and the pituitary body is closely related to that of the brain, and may conveniently be dealt with here. The epiblast in the angle formed by the cranial flexure becomes involuted as a hollow process situated in close proximity to the base of the brain. This hollow process is the mouth involution, and it is bordered on its posterior surface by the front wall of the alimentary tract, and on its anterior by the base of the fore-brain.

The uppermost end of this does not till near the close of stage K become markedly constricted off from the remainder, but is nevertheless the rudiment of the pituitary body. Pl. XVII,

figs. 9 *a* and 12 *m*, show in a most conclusive manner the correctness of the above account, and demonstrate that it is from the mouth involution, and not, as has usually been stated, from the alimentary canal, that the pituitary body is derived.

This fact was mentioned in my preliminary account of Elasmobranch development[1]; and has also been shown to be the case in Amphibians by Götte[2], and in Birds by Mihalkowics[3]. The fact is of considerable importance with reference to speculations as to the meaning of this body.

Plate XVII, fig. 7, represents a transverse section through the head during a stage between I and K; but, owing to the cranial flexure, it cuts the fore part of the head longitudinally and horizontally, and passes through both the fore-brain (*fb*) and the hind-brain (*iv. v.*). Close to the base of the fore-brain are seen the mouth (*m*), and the pituitary involution from this (*pt*). In contact with the pituitary involution is the blind anterior termination of the throat, which a little way back opens to the exterior by the first visceral cleft (I. *v.c.*). This figure alone suffices to demonstrate the correctness of the above account of the pituitary body; but the truth of this is still further confirmed by other figures on the same plate (fig. 9 *a* and 12 *m*); in which the mouth involution is in contact with, but still separated from, the front end of the alimentary tract. By the close of stage K, the septum between the mouth and throat becomes pierced, and the two are placed in communication. This condition is shown in Pl. XVII, fig. 16 *a*, and Pl. XVIII, fig. 1 *a*, 1 *c*, *pt*. In these figures the pituitary involution has become very partially constricted off from the mouth involution, though still in direct communication with it. In later stages the pituitary involution becomes longer and dilated terminally, while the passage connecting it with the mouth becomes narrower and narrower, and is finally reduced to a solid cord, which in its turn disappears. The remaining vesicle then becomes divided into lobes, and connects itself closely with the infundibulum (Pl. XVIII, figs. 5 and 6 *pt*). The later stages for Elasmobranchs are fully described by W. Müller in his im-

[1] *Quarterly Journal of Microscopic Science*, Oct. 1874.
[2] *Entwicklungsgeschichte der Unke.*
[3] *Arch. f. micr. Anat.* Vol. XI.

portant memoir on the Comparative Anatomy and development of this organ[1].

Development of the Cranial Nerves.

The present section deals with the whole development (so far as I have succeeded in elucidating it) of the cranial nerves (excluding the optic and olfactory nerves and the nerves of the eye-muscles) from their first appearance to their attainment of the adult condition. My description commences with the first development of the nerves, to this succeeds a short description of the nerves in the adult Scyllium, and the section is completed by an account of the gradual steps by which the adult condition is attained.

Before the close of stage H the more important of the cranial nerves make their appearance. The fifth and the seventh are the first to be formed. The fifth arises by stage G (Pl. XVII. fig. 3 V), near the anterior end of the hind-brain, as *an outgrowth from the extreme dorsal summit of the brain, in identically the same way as the dorsal root of a spinal nerve.*

The roots of the two sides sprout out from the summit of the brain, in contact with each other, and grow ventralwards, one on each side of the brain, in close contact with its walls. I have failed to detect more than one root for the two embryonic branches of the fifth (ophthalmic and mandibular), *and no trace of anterior or ventral root has been met with in any of my sections.*

The seventh nerve is formed nearly simultaneously with or shortly after the fifth, and some little distance behind and independently of it, opposite the anterior end of the thickening of the epiblast to form the auditory involution. It arises precisely like the fifth, from the extreme dorsal summit of the neural axis (Pl. XVII, fig. 4*a*, VII). So far as I have been able to determine, the auditory nerve and the seventh proper possess only a single root common to the two. There is no anterior root for the seventh any more than for the fifth.

Behind the auditory involution, at a stage subsequent to

[1] W. Müller, Ueber Entwicklung und Bau d. Hypophysis u. d. Processus infundibuli cerebri, *Jenaische Zeitschrift*, Bd. VI.

that in which the fifth and seventh nerves appear, there arise a series of roots from the dorsal summit of the hind-brain, which form the rudiments of the glosso-pharyngeal and vagus nerves. These roots are formed towards the close of stage H, but are still quite short at the beginning of stage I. Their manner of development resembles that of the previously described cranial nerves. The central ends of the roots of the opposite sides are at first in contact with each other, and there is nothing to distinguish the roots of the glosso-pharyngeal and of the vagus nerves from the dorsal roots of spinal nerves. Like the dorsal roots of the spinal nerves, they appear as a series of ventral prolongations of a continuous outgrowth from the brain, which outgrowth is moreover continuous with that for the spinal nerves[1]. The outgrowth of the vagus and glosso-pharyngeal nerves is not continuous with that of the seventh nerve. This is shown by Pl. XVII, figs. 4*a* and 4*b*. The outgrowth of the seventh nerve though present in 4*a* is completely absent in 4*b* which represents a section just behind 4*a*.

Thus, by the end of stage I, there have appeared the rudiments of the 5th, 7th, 8th, 9th and 10th cranial nerves, all of which spring from the hind-brain. These nerves all develope precisely as do the posterior roots of the spinal nerves, and it is a remarkable fact *that hitherto I have failed to find a trace in the brain of a root of any cranial nerve arising from the ventral corner of the brain as do the anterior roots of the spinal nerves*[2].

[1] In the presence of this continuous outgrowth of the brain from which spring the separate nerve stems of the vagus, may perhaps be found a reconciliation of the apparently conflicting statements of Götte and myself with reference to the vagus nerve. Götte regards the vagus as a single nerve, from its originating as an undivided rudiment; but it is clear from my researches that, for Elasmobranchs at least, this method of arguing will not hold good, since it would lead to the conclusion that all the spinal nerves were branches of one single nerve, since they too spring as processes from a continuous outgrowth from the brain!

[2] The conclusion here arrived at with reference to the anterior roots, is opposed to the observations of both Gegenbaur on Hexanchus, *Jenaische Zeitschrift*, Vol. VI, and of Jackson and Clarke on Echinorhinus, *Journal of Anatomy and Physiology*, Vol. X. These morphologists identify certain roots springing from the medulla below and behind the main roots of the vagus as true anterior roots of this nerve. The existence of these roots is not open to question, but without asserting that it is impossible for me to have failed to detect such roots had they been present in the embryo, I think I may maintain if these anterior roots are *not* present in the embryo, their identification as vagus roots must be abandoned; and they must be regarded as belonging to spinal nerves. This point is more fully spoken of at p. 471.

It is admittedly difficult to prove a negative, and it may still turn out that there are anterior roots of the brain similar to those of the spinal cord; in the mean time, however, the balance of evidence is in favour of there being none such. This at first sight appears a somewhat startling conclusion, but a little consideration shows that it is not seriously opposed to the facts which we know. In the first place it has been shown by myself[1] that in Amphioxus (whose vertebrate nature I cannot doubt) only dorsal nerve-roots are present. Yet the nerves of Amphioxus are clearly mixed motor and sensory nerves, and it appears to me far more probable that Amphioxus represents a phase of development in which the nerves had not acquired two roots, rather than one in which the anterior root has been lost. In other words, the condition of the nerves in Amphioxus appears to me to point to the conclusion *that primitively the cranio-spinal nerves of vertebrates were nerves of mixed function with one root only, and that root a dorsal one; and that the present anterior or ventral root is a secondary acquisition.* This conclusion is further supported by the fact that the posterior roots develope in point of time before the anterior roots. If it be admitted that the vertebrate nerves primitively had only a single root, then the retention of that condition in the brain implies that this became differentiated from the remainder of the nervous system at a very early period before the acquirement of anterior nerve-roots, and that these eventually become developed only in the case of spinal nerves, and not in the case of the already highly modified cranial nerves.

Subsequent Changes of the Nerves.—To simplify my description of the subsequent growth of the cranial nerves, I have inserted a short description of their distribution in the adult. This is taken from a dissection of Scyllium Stellare, which like other species has some individualities of its own not found in the other Elasmobranchs. For points not touched on in this description I must refer the reader to the more detailed accounts of my predecessors, amongst whom may specially be mentioned Stannius[2] for Carcharias, Spinax, Raja, Chimæra,

[1] *Journal of Anatomy and Physiology*, Vol. x.
[2] *Nervensystem d. Fische*, Rostock, 1849.

&c.; Gegenbaur[1] for Hexanchus; Jackson and Clarke[2] for Echinorhinus.

The ordinary nomenclature has been employed for the branches of the fifth and seventh nerves, though embryological data to be adduced in the sequel throw serious doubts upon it. Since I am without observations on the origin of the nerves to the muscles of the eyes, all account of these is omitted.

The fifth nerve arises from the brain by three roots[3]: (1) an anterior more or less ventral root; (2) a root slightly behind, but close to the former[4], formed by the coalescence of two distinct strands, one arising from a dorsal part of the medulla, and a second and larger from the ventral; (3) a dorsal and posterior root, in its origin quite distinct and well separated from the other two, and situated slightly behind the dorsal strand of the second root. This root a little way from its attachment becomes enclosed for a short distance in the same sheath as the dorsal part of the second root, and a slight mixture of fibres seems to occur, but the majority of its fibres have no connection with those of the second root. The first and second roots of the fifth appear to me partially to unite, but before their junction the ramus ophthalmicus profundus is given off from the first of them.

The fifth nerve, according to the usual nomenclature, has three main divisions. The first of these is the ophthalmic. It is formed by the coalescence of two entirely independent branches of the fifth, which unite on leaving the orbit. The dorsalmost of these, or ramus ophthalmicus superficialis, originates from the third and posterior of the roots of the fifth, nearly the whole of which appears to enter into its formation. This root is situated on the dorsal part of the "lobi trigemini," *at a point posterior to that of the other roots of the fifth or even of the seventh nerve.* The branch itself enters the orbit by a separate foramen, and, keeping on the dorsal side of it, reenters the cartilage at its anterior wall, and is there joined by the *ramus ophthalmicus profundus.* This latter nerve arises from the anterior root of the fifth, separately pierces the wall of the orbit, and takes a course slightly ventral to the superior ophthalmic nerve, but does not (as is usual with Elasmobranchs) run below the superior rectus and superior oblique muscles of the eye. The nerve formed by the coalescence of the superficial and deep ophthalmic branches courses a short way below the surface, and supplies the mucous canals of the front of the snout. It is a purely sensory nerve. Strong grounds will be adduced in the sequel for regarding the *ramus ophthalmicus superficialis*, though not the *ophthalmicus profundus*, as in reality a branch of the seventh, and not of the fifth nerve.

[1] *Jenaische Zeitschrift*, Vol. VI.

[2] *Journal of Anatomy and Physiology*, Vol. X.

[3] My results with reference to these roots accord exactly, so far as they go, with the more carefully worked out conclusions of Stannius, *loc. cit.* p. 29 and 30.

[4] The root of the seventh nerve cannot properly be distinguished from this root.

The second division of the fifth nerve is the superior maxillary, which appears to me to arise from both the first and second roots of the fifth, though mainly from the first. It divides once into two main branches. The first of these—the buccal nerve of Stannius—after passing forwards along the base of the orbit takes its course obliquely across the palatine arch and behind and below the nasal sack, supplying by the way numerous mucous canals, and dividing at last into two branches, one of these passing directly forwards on the ventral surface of the snout, and the second keeping along the front border of the mouth. The second division of the superior maxillary nerve (superior maxillary of Stannius), after giving off a small branch, which passes backwards in company with a branch from the inferior maxillary nerve to the levator maxillæ superioris, itself keeps close to the buccal nerve, and eventually divides into numerous fine twigs to the mucous canals of the skin at the posterior region of the upper jaw. It anastomoses with the buccal nerve. The inferior maxillary nerve arises mainly from the second root of the fifth. After sending a small branch to the levator maxillæ superioris, it passes outwards along the line separating the musculus adductor mandibulæ from the musculus levator labii superioris, and after giving branches to these muscles takes a course forward along the border of the lower jaw. It appears to be a mixed motor and sensory nerve.

The seventh or facial nerve arises by a root close to, but behind and below the second root of the fifth, and is intimately fused with this. It divides almost at once into a small anterior branch and large posterior.

The anterior branch is the palatine nerve. It gives off at first one or two very small twigs, which pursue a course towards the spiracle, and probably represent the spiracular nerves of other Elasmobranchs. Immediately after giving off these branches it divides into two stems, a posterior smaller and an anterior larger one. The former eventually takes a course which tends towards the angle of the jaw, and is distributed to the mucous membrane of the roof of the mouth, while the larger one bends forwards and supplies the mucous membrane at the edge of the upper jaw. The main stem of the seventh, after giving off a branch to the dorsal section of the musculus constrictor superficialis, passes outwards to the junction of the upper and lower jaws, where it divides into two branches, an anterior superficial branch, which runs immediately below the skin on the surface of the lower jaw, and a second branch, which takes a deep course along the posterior border of the lower jaw, between it and the hyoid, and sends a series of branches backwards to the ventral section of the musculus constrictor superficialis. The main stem of the facial is mixed motor and sensory. I have not noticed a dorsal branch, similar to that described by Jackson and Clarke.

The auditory nerve arises immediately behind the seventh, but requires no special notice here. A short way behind the auditory is situated the root of the glossopharyngeal nerve. This nerve takes an oblique course backwards through the skull, and gives off in its pas-

sage a very small dorsal branch, which passes upwards and backwards through the cartilage towards the roof of the skull. At the point where the main stem leaves the cartilage it divides into two branches, an anterior smaller branch to the hinder border of the hyoid arch, and a posterior and larger one to anterior border of the first branchial arch. It forks, in fact, over the first visceral cleft.

The vagus arises by a great number of distinct strands from the sides of the medulla. In the example dissected there were twelve in all. The anterior three of these were the largest; the middle one having the most ventral origin. The next four were very small and in pairs, and were separated by a considerable interval from the next four, also very small, and these again by a marked interval from the hindermost strand.

The common stem formed by the junction of these gives off immediately on leaving the skull a branch which forks on the second branchial cleft: a second for the third cleft is next given off; the main stem then divides into a dorsal branch — the lateral nerve — and a ventral one—the branchio-intestinal nerve—which, after giving off the branches for the two last branchial clefts, supplies the heart and intestinal tract. The lateral nerve passes back towards the posterior end of the body, internal to the lateral line, and between the dorso-lateral and ventro-lateral muscles. It gives off at its origin a fine nerve, which has a course nearly parallel to its own. The main stem of the vagus, at a short distance from its central end, receives a nerve which springs from the ventral side of the medulla, on about a level with the most posterior of the true roots of the vagus. This small nerve corresponds with the ventral or anterior roots of the vagus described by Gegenbaur, Jackson, and Clarke (though in the species investigated by the latter authors these roots did not join the vagus, but the anterior spinal nerves). Similar roots are also mentioned by Stannius, who found two of them in the Elasmobranchs dissected by him; it is possible that a second may be present in Scyllium, but have been overlooked by me, or perhaps may have been exceptionally absent in the example dissected.

The Fifth Nerve. The thinning of the roof of the brain, in the manner already described, produces a great change in the apparent position of the roots of all the nerves. The central ends of the rudiments of the two sides are, as has been mentioned, at first in contact dorsally; but, when by the growth of the roof of the brain its two lateral halves become pushed apart, the nerves also shift their position and become widely separated. The roots of the fifth nerve are so influenced by these changes that they spring from the brain about half way up its sides, and a little ventral to the border of its thin roof. While this change has been taking place in

the point of attachment of the fifth nerve, it has not remained in other respects in a stationary condition.

During stage H it already exhibits two distinct branches known as the mandibular and ophthalmic. These branches first lie outside a section of the body cavity which exists in the front part of the head. The ophthalmic branch of the fifth being situated near the anterior end of this, and the mandibular near the posterior end.

In stage I the body cavity in this part becomes divided into two parts one behind the other, the posterior being situated in the mandibular arch. The bifurcation of the nerve then takes place over the summit of the posterior of the two divisions of the body cavity, Pl. XVII, fig. 9 *b* v. and 10 v, &c., and at first both branches keep close to the sides of this.

The anterior or ophthalmic branch of the fifth soon leaves the walls of the cavity just spoken of and tends towards the eye, and there comes in close contact with the most anterior section of the body cavity which exists in the head. These relations it retains unchanged till the close of stage K. Between stages I and K it may easily be seen from the surface; but, before the close of stage K, the increased density of the tissues renders it invisible in the living embryo.

The posterior branch of the fifth extends downwards into the mandibular arch in close contact with the posterior and outer wall of the body space already alluded to. At first no branches from it can be seen, but I have detected by the close of stage K, by an examination of the living embryo, a branch springing from it a short way from its central extremity, and passing forwards, Pl. XVII, fig. 2 v. This branch I take to be the rudiment of the superior maxillary division of the fifth nerve. It is shown in section, Pl. XVII, fig. 15 *a* v.

In the stages after K the anatomy of the nerves becomes increasingly difficult to follow, and accordingly I must plead indulgence for the imperfections in my observations on all the nerves subsequently to this date. In the fifth I find up to stage O a single ophthalmic branch (Pl. XIX. fig. 4*b*), which passes forwards slightly dorsal to the eye and parallel and ventral to a branch of the seventh, which will be described when I come to that nerve. I have been *unable* to observe that this branch

divides into a ramus superficialis and ramus profundus, and subsequently to stage O I have no observations on it.

By stage O the fifth may be observed to have two very distinct roots, and a large ganglionic mass is developed close to their junction (Gasserian ganglion), Pl. XIX. fig. 4 *a*. But in addition to this ganglionic enlargement, all of the branches have special ganglia of their own, Pl. XIX. fig. 4 *b*.

Summary. The fifth nerve has almost from the beginning two branches, the ophthalmic (probably the inferior ophthalmic of the adult) and the inferior maxillary. The superior maxillary nerve arises later than the other two as a branch from the inferior, originating comparatively far from its root. There is at first but a single root for the whole nerve, which subsequently becomes divided into two. Ganglionic swellings are developed on the common stem and main branches of the nerve.

A general view of the nerve is shown in the diagram in Pl. XIX. fig. 1.

Seventh and Auditory Nerves.

There appears in my earliest sections a single large rudiment in the position of the seventh and auditory nerves; but in longitudinal sections of an embryo somewhat older than stage I, in which the auditory organ forms a fairly deep pit, still widely open to the exterior, there are to be seen immediately in front of the ear the rudiments of two nerves, which come into contact where they join the brain and have their roots still closely connected at the end of stage K (Pl. XVII. fig. 10 and 15 *a* and 15 *b*). The anterior of these pursues a straight course to the hyoid arch (Pl. XVII. fig. 10, VII.), the second of the two (Pl. XVII. fig. 10, *au. n.*), which is clearly the rudiment of the auditory nerve, developes a ganglionic enlargement and, turning backward, closely hugs the ventral wall of the auditory involution.

The observation just recorded appears to lead to the following conclusions with reference to the development of the auditory nerve. A single rudiment arises from the brain for

the auditory and seventh nerves. This rudiment subsequently becomes split into two parts, an anterior to form the seventh nerve, and a posterior to form the auditory nerve. The ganglionic part of the auditory nerve is derived from the primitive outgrowths from the brain, and not from the auditory involution. I do not feel perfectly confident that an independent origin of the auditory nerve might not have escaped my notice; but, admitting the correctness of the view which attributes to the seventh and auditory a common origin, it follows that the auditory nerve primitively arose in connection with the seventh, of which it may either, as Gegenbaur believes, be a distinct part—the ramus dorsalis—or else may possibly have formed part of a commissure, homologous with that uniting the dorsal roots of the spinal nerves, connecting the seventh with the glossopharyngeal nerve. In either case it must be supposed secondarily to have become separate and independent in consequence of the development of the organ of hearing.

My sections of embryos of stage K and the subsequent stages do not bring to light many new facts with reference to the auditory nerve: they demonstrate however that its ganglionic part increases greatly in size, and in stage O there is a distinct root for the auditory nerve in contact with that for the seventh.

The history of the seventh nerve in its later stages presents points of great interest. Near the close of stage K there may be observed, in the living embryos and in sections, two branches of the seventh in addition to the original trunk to the hyoid arch, both arising from its anterior side; one passes straight forwards close to the external skin, but is at first only traceable a short way in front of the fifth, and a second passes downwards into the mandibular arch in such a fashion, that the seventh nerve forks over the hyomandibular cleft (vide Pl. XVII. fig. 2, VII.; 15 *a*, VII.). My sections show both these branches with great clearness. A third branch has also come under my notice, whose course leads me to suppose that it supplies the roof of the palate.

In the later stages my attention has been specially directed to the very remarkable anterior branch of the seventh. This may, in stages L to O, be traced passing on a level with the

root of the fifth nerve above the eye, and apparently terminating in branches to the skin in front of the eye (Pl. XIX. fig. 3 *a*, 4 *a*, VII. *a*). It courses close beneath the skin (though this does not appear in the sections represented on account of their obliqueness), and runs parallel and dorsal to the ophthalmic branch of the fifth nerve, and may easily be seen in this position in longitudinal sections belonging to stage O; but its changes after this stage have hitherto baffled me, and its final fate is therefore, to a certain extent, a matter of speculation.

The two other branches of the seventh, viz., the hyoid or main branch and mandibular branch, retain their primitive arrangement till the close of stage O.

The fate of the remarkable anterior branch of the seventh nerve is one of the most interesting points which has started up in the course of my investigations on the development of the cranial nerves, and it is a matter of very great regret to me that I have not been able to clear up for certain its later history.

Its primitive distribution leads to the supposition that it becomes the nerve known in the adult as the *ramus ophthalmicus superficialis of the fifth nerve*, and this is the view which I admit myself to be inclined to adopt. There are several points in the anatomy of this nerve in the adult which tell in favour of accepting this view with reference to it. In the first place, the ramus ophthalmicus superficialis rises from the brain (vide description above, p. 460), quite independently of the ramus ophthalmicus profundus, and not in very close connection with the other branches of the fifth, and also considerably behind these, quite as far back indeed as the ventral root of the seventh. There is therefore nothing in the position of its root opposed to its being regarded as a branch of the seventh nerve. Secondly, its distribution, which might at first sight be regarded as peculiar, presents no very strange features if it is looked on as a ramus dorsalis of the seventh, whose apparent anterior instead of dorsal course is due to the cranial flexure. If, however, the distribution of the ramus ophthalmicus superficialis is used as an argument against my view, a satisfactory reply is to be found in the fact that a branch of the seventh nerve certainly has the distribution in question

in the embryo, and that there is no reason why it should not retain it *in the adult*.

Finally, the junction of the two rami ophthalmici, most remarkable if they are branches of a single nerve, would present nothing astonishing when they are regarded as branches of two separate nerves.

If this view be adopted, certain modifications of the more generally accepted views of the morphology of the cranial nerves will be necessitated; but this subject is treated of at the end of this section.

Some doubt hangs over the fate of the other branches of the seventh nerve, but their destination is not so obscure as that of the anterior branch. The branch to the roof of the mouth can be at once identified as the 'palatine nerve', and it only remains to speak of the mandibular branch.

It may be noticed first of all with reference to this branch, that the seventh behaves precisely like the less modified succeeding cranial nerves. It forks in fact over a visceral cleft (the hyomandibular) the two sides of which it supplies; the branch at the anterior side of the cleft is the later developed and smaller of the two. There cannot be much doubt that the mandibular branch must be identified with the spiracular nerve (præ-spiracular branch Jackson and Clarke) of the adult, and if the chorda tympani of Mammals is correctly regarded as the mandibular branch of the seventh nerve, then the spiracular nerve must represent it. Jackson and Clarke[1] take a different view of the homology of the chorda tympani, and regard it as equivalent to the ramus mandibularis internus (one of the two branches into which the seventh eventually divides), because this nerve takes its course over the ligament connecting the mandible with the hyoid. This view I cannot accept so long as it is admitted that the chorda tympani is the branch of a cranial nerve supplying the anterior side of a cleft. The ramus mandibularis internus, instead of forming with the main branch of the seventh a fork over the spiracle, passes to its destination completely behind and below the spiracle, and therefore fails to fulfil the conditions requisite for regarding it as a branch

[1] *Loc. cit.*

to the anterior wall of a visceral cleft. It is indeed clear that the ramus mandibularis internus cannot be identified with the embryonic mandibular branch of the seventh (which passes above the spiracle or hyomandibular cleft) when there is present in the adult another nerve (the spiracular nerve), which exactly corresponds in distribution with the embryonic nerve in question. My view accords precisely with that already expressed by Gegenbaur in his masterly paper on the nerves of Hexanchus, in which he distinctly states that he looks upon the spiracular nerve as the homologue of an anterior branchial branch of a division of the vagus. In the adult the spiracular nerve is sometimes represented by one or two branches of the palatine, *e.g.* Scyllium, but at other times arises independently from the main stem of the seventh[1]. The only difficulty in my identification of the embryonic mandibular branch with the adult spiracular nerve, is the extremely small size of the latter in the adult, compared with the size of mandibular in the embryo; but it is hardly surprising to find an atrophy of the spiracular nerve accompanying an atrophy of the spiracle itself. The palatine appears to me to have been rightly regarded by Jackson and Clarke as the great superficial petrosal of Mammals.

On the common root of the branches of the seventh nerve, as well as on its hyoid branch, ganglionic enlargements are present at an early period of development.

The Glossopharyngeal and Vagus Nerves. Behind the ear there are formed a series of five nerves which pass down to respectively the first, second, third, fourth and fifth visceral arches.

For each arch there is thus one nerve, whose course lies close to the posterior margin of the preceding cleft, a second anterior branch being developed later. These nerves are connected with the brain (as I have determined by transverse sections) by roots at first attached to the dorsal summit, but eventually situated about half-way down the sides (Pl. XVII. fig. 6), nearly opposite the level of the process which divides the ventricle of the hind-brain into a dorsal and a ventral moiety. The foremost of these nerves is the glosso-

[1] Hexanchus, Gegenbaur, *Jenaische Zeitschrift*, Vol. VI.

pharyngeal. The next four are, as has been shown by Gegenbaur[1], equivalent to four independent nerves, but form, together with the glossopharyngeal, a compound nerve, which we may briefly call the vagus.

This compound nerve by stage K attains a very complicated structure, and presents several remarkable and unexpected features. Since it has not been possible for me completely to elucidate the origin of all its various parts, it will conduce to clearness if I give an account of its structure during stage K or L, and then return to what facts I can mention with reference to its development. Its structure during these stages is represented on the diagram, Pl. XIX. fig. 1. There are present five branches, viz. the glossopharyngeal and four branches of the vagus, arising probably by a considerably greater number of strands from the brain[2]. All the strands from the brain are united together by a thin commissure, *Vg. com.*, continuous with the commissure of the posterior roots of the spinal nerves, and from this commissure the five branches are continued obliquely ventralwards and backwards, and each of them dilates into a ganglionic swelling. They all become again united together by a second thick commissure, which is continued backwards as the intestinal branch of the vagus nerve *Vg. in.* The nerves, however, are continued ventralwards each to its respective arch. From the hinder part of the intestinal nerve springs the lateral nerve *n.l.*, at a point whose relations to the branches of the vagus I have not certainly determined.

The whole nerve-complex formed by the glossopharyngeal and the vagus nerves cannot of course be shown in any single section. The various roots are shown in Pl. XIX. fig. 5. The dorsal commissure is represented in longitudinal section in Pl. XVII. fig. 15 *b*, *com.*, and in transverse section in Pl. XIX. fig. 2 *Vg*, *com.* The lower commissure continued as the intestinal nerve is shown in Pl. XVII. fig. 15 *a*, *Vg.*, and as seen in the living embryo in Pl. XVII. figs. 1 and 2. The ganglia are seen in Pl. XVII. fig. 6, *Vg.* My observations have not taught me much with reference to the origin of the two

[1] *Loc. cit.*
[2] In the diagram there are only five strands represented. This is due to the fact that I have not certainly made out their true number.

commissures, viz. the dorsal one and the one which forms the intestinal branch of the vagus. Very possibly they originate as a single commissure which becomes longitudinally segmented. It deserves to be noticed that the dorsal commissure has a long stretch, from the last branch of the vagus to the first spinal nerve, during which it is not connected with the root of any nerve; vide fig. 15 *b, com.* This space probably contained originally the now lost branches of the vagus. In many transverse sections where the dorsal commissure might certainly be expected to be present it cannot be seen, but this is perhaps due to its easily falling out of the sections. I have not been able to prove that the commissure is continued forwards into the auditory nerve.

The relation of the branches of the vagus and glossopharyngeal to the branchial clefts requires no special remark. It is fundamentally the same in the embryo as in the adult. The branches at the posterior side of the clefts are the first to appear, those at the anterior side of the clefts being formed subsequently to stage K.

One of the most interesting points with reference to the vagus is the number of separate strands from the brain which unite to form it. The questions connected with these have been worked out in a masterly manner, both from an anatomical and a theoretical standpoint, by Professor Gegenbaur[1]. It has not been possible for me to determine the exact number of these in my embryos, nor have I been able to show whether they are as numerous at the earliest appearance of the vagus as at a later embryonic period. The strands are connected (Pl. XIX. fig. 5) with separate ganglionic centres in the brain, though in several instances more than one strand is connected with a single centre. In an embryo between stage O and P more than a dozen strands are present. In an adult Scyllium I counted twelve separate strands, but their number has been shown by Gegenbaur to be very variable. Perhaps they are remnants of the roots of the numerous primary branches of the vagus which have now vanished; and this perhaps is the explanation of their variability, since in the case of all organs which are on the way to disappear variability is a precursor of disappearance.

[1] *Loc. cit.*

A second interesting point is the presence of the two connecting commissures spoken of above. It was not till comparatively late in my investigations that I detected the dorsal one. This has clearly the same characters as the dorsal commissure already described as connecting the roots of all the spinal nerves, and is indeed a direct prolongation of this. It becomes gradually thinner and thinner, and finally ceases to be observable by about the close of stage L. It is of importance as showing the similarity of the branches of the vagus to the dorsal roots of the spinal nerves. The ventral of the two commissures persists in the adult as the common stem from which all the branches of the vagus successively originate, and is itself continued backwards as the intestinal branch of the vagus. The glossopharyngeal nerve alone becomes eventually separated from the succeeding branches. Stannius and Gegenbaur have, as was mentioned above, detected in adult Elasmobranchs roots which join the vagus, and which resemble the anterior or ventral roots of spinal nerves; and I have myself described one such root in the adult Scyllium. I have searched for these in my embryos, but without obtaining conclusive results. In the earliest stages I can find no trace of them, but I have detected in stage L one anterior root on debatable border-land, which may conceivably be the root in question, but which I should naturally have put down for the root of a spinal nerve. Are the roots in question to be regarded as proper roots of the vagus, or as ventral roots of spinal nerves whose dorsal roots have been lost? The latter view appears to me the most probable one, partly from the embryological evidence furnished by my researches, which is clearly opposed to the existence of anterior roots in the brain, and partly from the condition of these roots in Echinorhinus, in which they join the succeeding spinal nerves and not the vagus[1]. The similar relations of the apparently homologous branch or branches in many Osseous Fish may also be used as an argument for my view.

If, as seems probable, the roots in question become the hypoglossal nerve, this nerve must be regarded as formed from the anterior roots of one or more spinal nerves. Without

[1] Vide Jackson and Clarke *loc. cit.* The authors take a different view to that here advocated, and regard the ventral roots described by them as having originally belonged to the vagus.

embryological evidence it does not however seem possible to decide whether the hypoglossal nerve contains elements only of anterior roots or of both anterior and posterior roots.

Mesoblast of the Head.

Body Cavity and Myotomes of the Head.—During stage F the appearance of a cavity on each side in the mesoblast of the head was described. These cavities end in front opposite the blind anterior extremity of the alimentary canal; behind they are continuous with the general body-cavity. I propose calling them *the head-cavities*. The cavities of the two sides have no communication with each other.

Coincidently with the formation of an outgrowth from the throat to form the first visceral cleft, the head-cavity on each side becomes divided into a section in front of the cleft and a section behind the cleft (vide Pl. XVII. fig. 4 *a* and 4 *b pp.*); and during stage H it becomes, owing to the formation of a second cleft, divided into three sections: (1) a section in front of the first or hyomandibular cleft; (2) a section in the hyoid arch between the hyomandibular cleft and the hyobranchial or first branchial cleft; (3) a section behind the first branchial cleft.

The section in front of the hyomandibular cleft stands in a peculiar relation to the two branches of the fifth nerve. The ophthalmic branch of the fifth lies close to the outer side of its anterior part, the mandibular branch close to the outer side of its posterior part. During stage I this front section of the head-cavity grows forward, and becomes divided, without the intervention of a visceral cleft, into an anterior and posterior division. The anterior lies close to the eye, and in front of the commencing mouth involution, and is connected with the ophthalmic branch of the fifth nerve. The posterior part lies completely within the mandibular arch, and is closely connected with the mandibular division of the fifth nerve.

As the rudiments of the successive visceral clefts are formed, the posterior part of the head-cavity becomes divided into successive sections, there being one section for each arch. Thus the whole head-cavity becomes on each side divided into (1) a premandibular section; (2) a mandibular section; (3) a hyoid section; (4) sections in the branchial arches.

The first of these divisions forms a space of a considerable size, with epithelial walls of somewhat short columnar cells. It is situated close to the eye, and presents a rounded or sometimes triangular figure in sections (Pl. XVII. fig. 7, 9 *b* and 16 *b*, I. *pp.*). The ophthalmic branch of the fifth nerve passes close to its superior and outer wall.

Between stages I and K the anterior cavities of the two sides are prolonged ventralwards and meet below the base of the fore-brain (Pl. XVII. fig. 8, I. *pp.*). The connection between the two cavities appears to last for a considerable time, and still persists at the close of stage L. The anterior or premandibular pair of cavities are the only parts of the body-cavity within the head which unite ventrally. In the trunk, however, the primitively independent lateral halves of the body-cavity always unite in this way. The section of the head-cavity just described is so similar to the remaining posterior sections that it must be considered as equivalent to them.

The next division of the head-cavity, which from its position may be called the mandibular cavity, presents during the stages I and K a spatulate shape. It forms a flattened cavity, dilated dorsally, and produced ventrally into a long thin process parallel to the hyomandibular gill-cleft, Pl. XVII. fig. 1 *pp.* and fig. 7, 9 *b* and 15 *a*, 2 *pp.* Like the previous space it is lined by a short columnar epithelium.

The fifth nerve, as has already been mentioned, bifurcates over its dorsal summit, and the mandibular branch of that nerve passes down on its posterior and outer side. The mandibular aortic arch is situated close to its inner side, Pl. XVII. fig. 7. Towards the close of this period the upper part of the cavity atrophies. Its lower part also becomes much narrowed, but its walls of columnar cells persist and lie close to one another. The outer or somatic wall becomes very thin indeed, the splanchnic wall, on the other hand, thickens and forms a layer of several rows of elongated cells. This thicker wall is on its inner side separated from the surrounding tissue by a small space lined by a membrane-like structure. In each of the remaining arches there is a segment of the original body-cavity fundamentally similar to that in the mandibular arch. A dorsal dilated portion appears, however, to be present in the

third or hyoid section alone, and even there disappears by the close of stage K. The cavities in the posterior parts of the head become much reduced like those in its anterior part, though at rather a later period. Their walls however persist, and become more columnar. In Pl. XVII. fig. 13 *b*, *pp*., is represented the cavity in the last arch but one, at a period when the cavity in the mandibular arch has become greatly reduced. It occupies the same position on the outer side of the aortic trunk of its arch as does the cavity in the mandibular arch (Pl. XVII. fig. 7, 2*pp*). In Torpedo embryos the head-cavity is much smaller, and atrophies earlier than in the embryos of Pristiurus and Scyllium.

It has been shown that, with the exception of the most anterior, the divisions of the body-cavity in the head become atrophied, *not so however their walls*. The cells forming these become elongated, and by stage N become distinctly developed into muscles. Their exact history I have not followed in its details, but they unquestionably become the musculus constrictor superficialis and musculus interbranchialis[1]; and probably also musculus levator mandibuli and other muscles of the front part of the head.

The most anterior cavity close to the eye remains unaltered much longer than the remaining cavities, and its two halves are still in communication at the close of stage L. I have not yet succeeded in tracing the subsequent fate of its walls, but think it probable that they develope into the muscles of the eye. The morphological importance of the sections of the body-cavity in the head cannot be over-estimated, and the fact that the walls become developed into the muscular system of the head renders it almost certain *that we must regard them as equivalent to the muscle-plates of the body, which originally contain, equally with those of the head, sections of the body-cavity.* If this determination is correct, there can be no doubt that they ought to serve as valuable guides to the number of segments which have coalesced to form the head. This point is, however, discussed in a subsequent section.

General mesoblast of the head.—In stage G no mesoblast is

[1] Vide Vetter, *Die Kiemen und Kiefermusculatur d. Fische. Jenaische Zeitschrift*, Vol. VII.

present in the head, except that which forms the walls of the head-cavity.

During stage H a few cells of undifferentiated connective tissue appear around the stalk of the optic vesicle, and in the space between the front end of the alimentary tract and the base of the brain in the angle of the cranial flexure. They are probably budded off from the walls of the head-cavities. Their number rapidly increases, and they soon form an investment surrounding all the organs of the head, and arrange themselves as a layer, between the walls of the roof of the fore and mid-brain and the external skin. At the close of stage K they are still undifferentiated and embryonic, each consisting of a large nucleus surrounded by a very delicate layer of protoplasm produced into numerous thread-like processes. They form a regular meshwork, the spaces of which are filled up by an intercellular fluid.

I have not worked out the development of the cranial and visceral skeleton; but this has been made the subject of an investigation by Mr Parker, who is more competent to deal with it than any other living anatomist. His results were in part made known in his lectures before the Royal College of Surgeons[1].

All my efforts have hitherto failed to demonstrate any segmentation in the mesoblast of the head, other than that indicated by the sections of the body-cavity before mentioned; but since these, as above stated, must be regarded as equivalent to muscle-plates, any further segmentation of mesoblast could not be anticipated. To this statement the posterior part of the head forms an apparent exception. Not far behind the auditory involution there are visible at the end of period K a few longitudinal muscles, forming about three or four muscle-plates, the ventral part of which is wanting. I have not the means of deciding whether they properly belong to the head, or may not really be a part of the trunk system of muscles which has, to a certain extent, overlapped the back part of the head, but am inclined to accept the latter view. These cranial muscle-plates are shown in Pl. XVII. fig. 15 *b*, and in Pl. XIX. fig. 2.

[1] A report of the lectures appeared in *Nature*.

Notochord in the Head.—The notochord during stage G is situated for its whole length close under the brain, and terminates opposite the base of the mid-brain. As the cranial flexure becomes greater and mesoblast is collected in the angle formed by this, the termination of the notochord recedes from the base of the brain, but remains in close contact with the front end of the alimentary canal. At the same time its terminal part becomes very much thinner than the remainder, ends in a point, and exhibits signs of a retrogressive metamorphosis. It also becomes bent upon itself in a ventral direction through an angle of 180°; vide Pl. XVII. fig. 9 *a* and 16 *a*. In some cases this curvature is even more marked than is represented in these figures.

The bending of the end of the notochord is not directly caused by the cranial flexure, as is proved by the fact that the end of the notochord becomes bent through a far greater angle than does the brain. During the stages subsequent to K the ventral flexure of the notochord disappears, and its terminal part even becomes bent slightly dorsalwards.

Hypoblast of the head.—The only feature of the alimentary tract in the head which presents any special interest is the formation of the gill-slits and of the thyroid body. In the present section the development of the former alone is dealt with: the latter body will be treated in the section devoted to the general development of the alimentary tract.

The gill-slits arise as outgrowths of the lining of the throat towards the external skin. In the gill-slits of Torpedo I have observed a slight ingrowth of the external skin towards the hypoblastic outgrowth in one single case. In all other cases observed by me, the outgrowth from the throat meets the passive external skin, coalesces with it, and then, by the dissolution of the wall separating the lumen of the throat from the exterior, a free communication from the throat outwards is effected; vide Pl. XVII. fig. 5 *a* and *b*, and 13 *b*. Thus it happens that the walls lining the clefts are entirely formed of hypoblast. The clefts are formed successively[1], the anterior appearing first, and it is not till after the rudiments of three have appeared, that any of them become open to the exterior.

[1] Vide *Journal of Anatomy and Physiology*, Vol. X. Pl. XXIV. and XXV.

In stage K, four if not five are open to the exterior, and the rudiments of six, the full number, have appeared[1]. Towards the close of stage K there arise, from the walls of the 2nd, 3rd, and 4th clefts, very small knob-like processes, the rudiments of the external gills. These outgrowths are formed both by the lining of the gill-cleft and by the adjoining mesoblast[2].

From the mode of development of the gill-clefts, it appears that their walls are lined externally by hypoblast, and therefore that the external gills are processes of the walls of the alimentary tract, *i.e.* are covered by an hypoblastic, and not an epiblastic layer. It should be remembered, however, that after the gill-slits become open, the point where the hypoblast joins the epiblast ceases to be determinable, so that some doubt hangs over the above statement.

The identification of the layer to which the gills belong is not without interest. If the external gills have an epiblastic origin, they may be reasonably regarded[3] as homologous with the external gills of Annelids; but, if derived from the hypoblast, this view becomes, to say the least, very much less probable.

Segmentation of the Head.—The nature of the vertebrate head and its relation to the trunk forms some of the oldest questions of Philosophical Morphology.

The answers of the older anatomists to these questions are of a contradictory character, but within the last few years it has been more or less generally accepted that the head is, in part at least, merely a modified portion of the trunk, and composed, like that, of a series of homodynamous segments[4]. While the researches of Huxley, Parker, Gegenbaur, Götte, and other anatomists, have demonstrated in an approximately conclusive manner that the head is composed of a series of segments, great divergence of opinion still exists both as to the number of these segments, and as to the modifications which they have undergone, especially

[1] The description of stage K and L, Vol. x. p. 562, is a little inaccurate with reference to the number of the visceral clefts, though the number visible in the hardened embryos is correctly described.

[2] Vide on the development of the gills, Schenk, *Sitz. d. k. Akad. Wien*, Vol. LXXI., 1875.

[3] Vide Dohrn, *Ursprung d. Wirbelthiere.*

[4] Semper, in his most recent work, maintains, if I understand him rightly, that the head is in no sense a modified part of the trunk, but admits that it is segmented in a similar fashion to the trunk.

in the anterior part of the head. The questions involved are amongst the most difficult in the whole range of morphology, and the investigations recorded in the preceding pages do not, I am very well aware, go far towards definitely solving them. At the same time my observations on the nerves and on the head-cavities appear to me to throw a somewhat new light upon these questions, and it has therefore appeared to me worth while shortly to state the results to which a consideration of these organs points. There are three sets of organs, whose development has been worked out, each of which presents more or less markedly a segmental arrangement:—(1) The cranial nerves; (2) the visceral clefts; (3) the divisions of the head-cavity.

The first and second of these have often been employed in the solution of the present problem, while the third, so far as is known, exists only in the embryos of Elasmobranchs.

The development of the cranial nerves has recently been studied with great care by Dr Götte, and his investigations have led him to adopt very definite views on the segments of head. The arrangement of the cranial nerves *in the adult* has frequently been used in morphological investigations about the skull, but there are to my mind strong grounds against regarding it as affording a safe basis for speculation. The most important of these depends on the fact that nerves are liable to the greatest modification on any changes taking place in the organs they supply. On this account it is a matter of great difficulty, amounting in many cases to actual impossibility, to determine the morphological significance of the different nerve-branches, or the nature of the fusions and separations which have taken place at the roots of the nerves. It is, in fact, only in those parts of the skull which have, relatively speaking, undergone but slight modifications, and which require no special elucidation from the nerves, that these sufficiently retain in the adult their primitive form to serve as trustworthy morphological guides.

I propose to examine separately the light thrown on the segmentation of the head by the development of (1) the nerves, (2) the visceral clefts, (3) the head-cavities; and then to compare the three sets of results so obtained.

The post-auditory nerves present no difficulties; they are all organized in the same fashion, and, as was first pointed out by

Gegenbaur, form five separate nerves, each indicating a segment. A comparison of the post-auditory nerves of Scyllium and other typical Elasmobranchs with those of Hexanchus and Heptanchus proves, however, that other segments were originally present behind those now found in the more typical forms. And the presence in Scyllium of numerous (twelve) strands from the brain to form the vagus, as well as the fact that a large section of the commissure connecting the vagus roots with the posterior roots of the spinal nerves is not connected with the brain, appear to me to show that all traces of the lost nerves have not yet vanished.

Passing forwards from the post-auditory nerves, we come to the seventh and auditory nerves. The embryological evidence brought forward in this paper is against regarding these nerves as representing two segments. Although it must be granted that my evidence is not conclusive against an independent formation of these two nerves, yet it certainly tells in favour of their originating from a common rudiment, and Marshall's results on the origin of the two nerves in Birds (published in the present number of this *Journal*) support, I have reason to believe, the same conclusion. Even were it eventually to be proved that the auditory nerve originated independently of the seventh, the general relations of this nerve, embryological and otherwise, are such that, provisionally at least, it could not be regarded as belonging to the same category as the facial or glossopharyngeal nerves, and it has therefore no place in a discussion on the segmentation of the head.

The seventh nerve of the embryo (Pl. XIX. fig. 1, VII.) is formed by the junction of three conspicuous branches, (1) an anterior dorsal branch which takes a more or less horizontal course above the eye (VII. *a*); (2) a main branch to the hyoid arch (VII. *hy*); (3) a smaller branch to the posterior edge of the mandibular arch (VII. *mn*). The first of these branches can clearly be nothing else but the typical "ramus dorsalis," of which however the auditory may perhaps be a specialized part. The fact that this branch pursues an anterior and not a directly dorsal course is probably to be explained as a consequence of the cranial flexure. The two other branches of the seventh nerve are the same as those present in all the

posterior nerves, viz. the branches to the two sides of a branchial cleft, in the present instance the spiracle; the seventh nerve being clearly the nerve of the hyoid arch.

The fifth nerve presents in the arrangement of its branches a similarity to the seventh nerve so striking that it cannot be overlooked. This similarity is at once obvious from an inspection of the diagram of the nerves on Pl. XIX. fig. 1, V., or from an examination of the sections representing these nerves (Pl. XIX. figs. 3 and 4). It divides like the seventh nerve into three main branches: (1) an anterior and dorsal branch (*r.* ophthalmicus profundus), whose course lies parallel to but ventral to that of the dorsal branch of the seventh nerve; (2) a main branch to the mandibular arch (*r.* maxillæ inferioris); and (3) an anterior branch to the palatine arcade (*r.* maxillæ superioris). I was at first inclined to regard the anterior branch of the fifth (ophthalmic) as representing a separate nerve, and was supported in this view by its relation to the most anterior of the head-cavities; but the unexpected discovery of an exactly *similar branch* in the seventh nerve has induced me to modify this view, and I am now constrained to view the fifth as a single nerve, whose branches exactly correspond with those of the seventh. The anterior branch of the fifth is, like the corresponding branch of the seventh, the *ramus dorsalis*, and the two other branches are the equivalent of the branches of the seventh, which fork over the spiracle, though in the case of the fifth nerve no distinct cleft is present unless we regard the mouth as such. Embryology thus appears to teach us that the fifth nerve is a single nerve supplying the mandibular arch, and not, as has been usually thought, a complex nerve resulting from the coalescence of two or three distinct nerves. My observations do not embrace the origin or history of the third, fourth, and sixth nerves, but it is hardly possible to help suspecting that in these we have the nerve of one or more segments in front of that supplied by the fifth nerve; a view which well accords with the most recent morphological speculations of Professor Huxley[1].

From this enumeration of the nerves the optic nerve is

[1] Preliminary note upon the brain and skull of Amphioxus, *Proc. of the Royal Society*, Vol. XXII.

excluded for obvious reasons, and although it has been shown above that the olfactory nerve developes like the other nerves as an outgrowth from the brain, yet its very late appearance and peculiar relations are, at least for the present, to my mind sufficient grounds for excluding it from the category of segmental cranial nerves.

The nerves then give us indications of seven cranial segments, or, if the nerves to the eye-muscles be included, of *at the least* eight segments, but to these must be added a number of segments now lost, but which once existed behind the last of those at present remaining.

The branchial clefts have been regarded as guides to segmentation by Gegenbaur, Huxley, Semper, etc., and this view cannot I think be controverted. In Scyllium there are six clefts which give indications of seven segments, viz. the segments of the mandibular arch, hyoid arch, and of the five branchial arches. If, following the views of Dr Dohrn[1], we regard the mouth as representing a cleft, we shall have seven clefts and eight segments; and it is possible, as pointed out in Dr Dohrn's very suggestive pamphlet, that remnants of a still greater number of præoral clefts may still be in existence. Whatever may be the value of these speculations, such forms as Hexanchus and Heptanchus and Amphioxus make it all but certain that the ancestors of vertebrates had a number of clefts behind those now developed.

The last group of organs to be dealt with for our present question is that of the Head-Cavities.

The walls of the spaces formed by cephalic prolongations of the body-cavity develope into muscles and resemble the muscle-plates of the trunk, and with these they must be identified, as has been already stated. As equivalent to the muscle-plates, they clearly are capable of serving as very valuable guides for determining the segmentation of the head. There are then a pair of these in front of the mandibular arch, a pair in the mandibular arch, and a pair in each succeeding arch. In all there are eight pairs of these cavities representing eight segments, the first of them præoral. As was mentioned above, each of the sections of the head-cavity (except perhaps the

[1] *Ursprung d. Wirbelthiere.*

first) stands in a definite relation to the nerve and artery of the arch in which it is situated.

The comparative results of these three independent methods of determining the segmentation of the head are in the subjoined table represented in a form in which they can be compared:—

Table of the Cephalic Segments as determined by the Nerves, Visceral Arches, and Head-Cavities.

Segments.	Nerves.	Visceral Arches.	Head-Cavities.
Præoral 1	3rd and 4th and ? 6th nerves (perhaps representing more than one segment)	(?)	1st head-cavity (in my figures 1 *pp.*)
Postoral 2	5th nerve	Mandibular	2nd head-cavity (in my figures 2 *pp.*)
—— 3	7th nerve	Hyoid	3rd head-cavity
—— 4	Glossopharyngeal nerve	1st branchial arch	4th head-cavity
—— 5	1st branch of vagus	2nd branchial arch	5th head-cavity
—— 6	2nd branch of vagus	3rd branchial arch	6th head-cavity
—— 7	3rd branch of vagus	4th branchial arch	7th head-cavity
—— 8	4th branch of vagus	5th branchial arch	8th head-cavity

In the above table the first column denotes the segments of the head as indicated by a comparison of the three sets of organs employed. The second column denotes the segments as obtained by an examination of the nerves; the third column is for the visceral arches (which lead to the same results as, but are more convenient for our table than, the visceral clefts), and the fourth column is for the head-cavities. It may be noticed that from the second segment backwards the three sets of organs lead to the same results. The head-cavities indicate one segment in front of the mouth, and now that the ophthalmic branch of the fifth has been dethroned from its position as a separate nerve, the eye-nerves, or one of them, may probably be regarded as belonging to this segment. If the suggestion made above (p. 474), that the walls of the first cavity become the eye-muscles, be correct, the eye-nerves would perhaps after all be the most suitable nerves to regard as belonging to the segment of the first head-cavity.

EXPLANATION OF PLATE XV.

Complete list of reference letters.

ep. epiblast. *sp. c.* spinal cord. *l l.* lateral line.
m. c. mucous canal of the head. *n. l.* nervus lateralis.
v. in. intestinal branch of the vagus. *v. op.* ramus ophthalmicus of the fifth nerve.
m. p. muscle-plate. *m. p'.* muscles of muscle-plate.
v. ar. vertebral arch. *na.* neural arch. *ha.* hæmal arch.
rp. rib process. *m. el.* membrana elastica externa.
v b. vertebral body. *ch.* notochord. *sh.* sheath of notochord.
x. sub-notochordal rod. *sy. g.* sympathetic ganglion.
s. d. segmental duct. *l.* liver. *al.* alimentary tract.
um. umbilical duct. *ao.* aorta. *ca v.* cardinal vein.
v. cau. caudal vein. *v.* blood-vessel. *c.* connective tissue.

Fig. 1. Section through the anterior part of an embryo of *Scyllium canicula* during stage L.
c. Peculiar large cells which are found at the dorsal part of the spinal cord. Sympathetic ganglion shown at *sy. g.* Zeiss A, ocul. 1.

Fig. 2. Section through the lateral line at the time of its first formation. The cells marked *n. l.* were not sufficiently distinct to make it quite certain that they really formed part of the lateral nerve. Zeiss B, ocul. 2.

Fig. 3*a*. 3*b*. 3*c*. 3*d*. Four sections of the lateral line from an embryo belonging to stage L. 3*a* is the most anterior. In 3*a* the lateral nerve (*n. l.*) is seen to lie in the mesoblast at some little distance from the lateral line. In 3*b* and 3*c* it lies in immediate contact with and partly enclosed by the modified epiblast cells of the lateral line. In 3*d*, the hindermost section, the lateral line is much larger than in the other sections, but no trace is present of the lateral nerve. The sections were taken from the following slides of my series of the embryo (the series commencing at the tail end) 3*d* (46). 3*c* (64). 3*b* (84). 3*a* (93). The figures all drawn on the same scale, but 3*a* is not from the same side of the body as the other sections.

Fig. 4. Section through lateral line of an embryo of stage P at the point where it is acquiring an opening to the exterior. The peculiar modified cells of its innermost part deserve to be noticed. Zeiss D, ocul. 2.

Fig. 5. Mucous canals of the head with branches of the ramus ophthalmicus growing towards them. Stage O. Zeiss A, ocul. 2.

Fig. 6. Mucous canals of head with branches of the ramus ophthalmicus growing towards them. Stage between O and P. Zeiss *aa*, ocul. 2.

Fig. 7. Junction of a nerve and mucous canal. Stage P. Zeiss D, ocul. 2.

Fig. 8. Longitudinal and horizontal section through the muscle-plates and adjoining structures at a stage intermediate between L and M. The section is intended to show the gradual conversion of the cells of the somatic layer of muscle-plates into muscles.

Fig. 9. Longitudinal section through the notochord and adjoining parts to show the first appearance of the cartilaginous notochordal sheath which forms the vertebral centra. Stage N.

Fig. 10. Transverse section through the tail of an embryo of stage P to show the coexistence of the rib-process and hæmal arch in the first few sections after the appearance of the latter. Zeiss C, ocul. 1.

Fig. 11. Transverse section through the centre of a caudal vertebra of an embryo somewhat older than Q. It shows (1) the similarity between the arch-tissue and the hyaline tissue of the outer layer of the vertebral centrum, and (2) the separation of the two by the membrana elastica externa. (*m. el*) It shows also the differentiation of three layers in the vertebral centrum: vide p. 419.

EXPLANATION OF PLATE XVI.

Complete list of reference letters.

p r. posterior root of a spinal nerve.
a r. anterior root of a spinal nerve. *n.* spinal nerve.
sp g. ganglion on posterior root of spinal nerve.
com. commissure connecting the posterior roots of the spinal nerves.
w. white matter of spinal cord. *n. c.* neural canal.
y. point where the spinal cord became segmented off from the superjacent epiblast.
i. mesoblastic investment of spinal cord. *m. p.* muscle-plate.
v.r. vertebral rudiment.

Fig. 1, 2, and 3. Three sections of a Pristiurus embryo belonging to stage I. Fig. 1 passes through the heart, fig. 2 through the anterior part of the dorsal region, fig. 3 through a point slightly behind this. (Zeiss CC, ocul. 2.) In fig. 3 there is visible a slight proliferation of cells from the dorsal summit of the neural canal. In fig. 2 this proliferation definitely constitutes two club-shaped masses of cells (*p r*)—the rudiments of the posterior nerve-roots,—both attached to the dorsal summit of the spinal cord. In fig. 1 the rudiments of the posterior roots are of considerable length.

Fig. 4. Section through the dorsal region of a Torpedo embryo slightly older than stage I, with three visceral clefts. (Zeiss CC, ocul. 2.) The section shows the formation of a pair of dorsal nerve-rudiments (*p r*) and a ventral nerve-rudiment (*a r*). The latter is shown in its youngest condition, and is not distinctly cellular.

Fig. 5. Section through the dorsal region of a Torpedo embryo slightly younger than stage K. (Zeiss CC, ocul. 2.) The connective-tissue cells are omitted. The rudiment of the ganglion (*sp. g.*) on the posterior root has appeared, and the junction of posterior root with the cord is difficult to detect. The anterior root forms an elongated cellular structure.

Fig. 6. Section through the dorsal region of a Pristiurus embryo of stage K. (Zeiss CC, ocul. 2.) The section especially illustrates the attachment of the posterior root to the spinal cord.

Fig. 7. Section through the same embryo as fig. 6. (Zeiss CC, ocul. 1.) The section contains an anterior root, which takes its origin at a point opposite the interval between two posterior roots.

Fig. 8. A series of posterior roots united by a dorsal commissure, from a longitudinal and vertical section of a Scyllium embryo belonging to a stage intermediate between L and M. The embryo was hardened in a mixture of osmic and chromic acids.

Fig. 9. The central end of a posterior nerve-root from the same embryo, with the commissure springing out from it on either side.

EXPLANATION OF PLATE XVII.

THE HEAD DURING STAGES G—K.

Complete list of references.

e p. external epiblast. *op.* eye. *op. v.* optic vesicle.
op. n. optic nerve. *l.* lens. *Ch.* choroid slit.
hy. hyaloid membrane. *ol.* olfactory pit. *au. v.* auditory vesicle.
au. n. auditory nerve. *au. p.* auditory pit.
au. thickening of epiblast to form the auditory pit.
f b. fore-brain. *cer.* cerebrum. *pn.* pineal gland.
pt. pituitary body. *In.* infundibulum.
m b. mid-brain. *b b.* base of brain. *b.* wall of brain.
h b. hind-brain. *cb.* cerebellum. iv. *v.* fourth ventricle.
sp. c. spinal cord.
v. fifth nerve. *opth.* v. ophthalmic branch of fifth. *mn.* v. mandibular branch of fifth. vii. seventh or facial nerve. *gl.* glossopharyngeal nerve. *com.* commissure connecting roots of vagus nerve.
Vg. vagus. *p.* posterior root of spinal nerve.
1, 2 etc. *p p.* first, second, etc. section of body cavity in the head.
ch. notochord.
m. mesoblast at the base of the brain.
ht. heart. *V. c.* visceral cleft. 1, 2, 3 etc. *e.g.* external gills.
al. alimentary canal. *Th.* thyroid body.
ao. aorta. 1 *a. a.* 2 *a. a.* etc. 1st, 2d, etc. aortic arch.
a. c. v. anterior cardinal vein. *v.* blood-vessel.
M. mouth involution.
so. somatopleure. *sp.* splanchnopleure.

Fig. 1. Head of a Pristiurus embryo of stage K viewed as a transparent object.

The points which deserve special attention are: (1) The sections of the body cavity in the head (*pp.*). The first or premandibular section being situated close to the eye. The second in the mandibular arch. Above this one the fifth nerve bifurcates. The third at the summit of the hyoid arch.

The cranial nerves and the general appearance of the brain are well shown in the figure.

The notochord cannot be traced in the living embryo so far forward as it is represented. It has been inserted according to the position which it is seen to occupy in sections.

Fig. 2. Head of an embryo of Scyllium canicula somewhat later than stage K, viewed as a transparent object.

The figure shows the condition of the brain; the branches of the fifth and seventh nerves (v. vii.); the rudiments of the semicircular canals; and the commencing appearance of the external gills as buds on both walls of 2nd, 3rd, and 4th clefts. The external gills have not appeared on first cleft or spiracle.

Fig. 3. Section through the head of a Pristiurus embyro during stage G. It shows (1) the fifth nerve (v.) arising as an outgrowth from the dorsal summit of the brain. (2) The optic vesicles not yet constricted off from the fore-brain.

Fig. 4 *a* and 4 *b*. Two sections through the head of a Pristiurus embryo of stage I. They show (1) the appearance of the seventh nerve. (2) The

portion of the body cavity belonging to the first and second visceral arches. (3) The commencing thickening of epiblast to form the auditory involution.

In 4 *b*, the posterior of the two sections, no trace of an auditory nerve is to be seen.

Fig. 5 *a* and 5 *b*. Two sections through the head of a Torpedo embryo with 3 visceral clefts. Zeiss A, ocul. 1.

5 *a* shows the formation of the thin roof of the fourth ventricle by a divarication of the two lateral halves of the brain.

Both sections show the commencing formation of the thyroid body (*th*) at the base of the mandibular arch.

They also illustrate the formation of the visceral clefts by an outgrowth from the alimentary tract without any corresponding ingrowth of the external epiblast.

Fig. 6. Section through the hind-brain of a somewhat older Torpedo embryo. Zeiss A, ocul. 1.

The section shows (1) the attachment of a branch of the vagus to the walls of the hind-brain. (2) The peculiar form of the hind-brain.

Fig. 7. Transverse section through the head of a Pristiurus embryo belonging to a stage intermediate between I and K, passing through both the fore-brain and the hind-brain. Zeiss A, ocul. 1.

The section illustrates (1) the formation of the pituitary body (*pt*) from the mouth involution (*m*), and proves that, although the wall of the throat (*al*) is in contact with the mouth involution, there is by this stage no communication between the two.

The section illustrates (1) The eye. (2) The sections of the body cavity in the head, 1 *pp*. 2 *pp*. (3) The fifth nerve (v.) and the seventh nerve (vii.).

Fig. 8. Transverse section through the brain of a rather older embryo than fig. 7. It shows the ventral junction of the anterior sections of the body cavity in the head, 1 *pp*.

Fig. 9 *a* and 9 *b*. Two longitudinal sections through the brain of a Pristiurus embryo belonging to a stage intermediate between I and K. (Zeiss A, ocul. 1.)

Fig. 9 *a*. Is taken through the median line, but is reconstructed from two sections. It shows (1) The divisions of the brain—The cerebrum and thalamencephalon in the fore-brain; the mid-brain; the commencing cerebellum in the hind-brain. (2) The relation of the mouth involution to the infundibulum. (3) The termination of the notochord.

Fig. 9 *b*. Is a section to one side of the same brain. It shows (1) The divisions of the brain. (2) The point of outgrowth of the optic nerves, *op. n*. (3) The sections of the body cavity in the head and the bifurcation of the optic nerve over the 2nd of these.

Fig. 10. Longitudinal section through the head of a Pristiurus embryo somewhat younger than fig. 9. Zeiss a, ocul. 4. It shows the relation of the nerves and the junction of the fifth, seventh, and auditory nerves with the brain.

Fig. 11. Longitudinal section through the fore-brain of a Pristiurus embryo of stage K, slightly to one side of the middle line. It shows the deep constriction separating the thalamencephalon from the cerebral hemispheres.

Fig. 12. Longitudinal section through the base of the brain of an embryo of a stage intermediate between I and K.

It shows (1) The condition of the end of the notochord. (2) The relation of mouth involution to the infundibulum.

Fig. 13 *a.* Longitudinal and horizontal section through part of the head of a Pristiurus embryo rather older than K. Zeiss A, ocul. 1.

The figure contains the eye cut through in the plane of the choroid slit. Thus the optic nerve (*op. n*) and choroid slit (*ch*) are both exhibited. Through the latter is seen passing mesoblast accompanied by a blood-vessel (*v*). *Op* represents part of the optic vesicle to one side of the choroid slit.

No mesoblast can be seen passing round the outside of the optic cup; and the only mesoblast which enters the optic cup passes through the choroid slit.

Fig. 13 *b.* Transverse section through the last arch but one of the same embryo as 13 *a.* Zeiss A, ocul. 1.

The figure shows (1) The mode of formation of a visceral cleft without any involution of the external skin. (2) The head cavity in the arch and its situation in relation to the aortic arch.

Fig. 14. Surface view of the nasal pit of an embryo of same age as fig. 13. The specimen was prepared by removing the nasal pit, flattening it out and mounting in glycerine after treatment with chromic acid. It shows the primitive arrangement of the Schneiderian folds. One side has been injured.

Fig. 15 *a* and 15 *b.* Two longitudinal and vertical sections through the head of a Pristiurus embryo belonging to stage K. Zeiss a, ocul. 3.

Fig. 15 *a* is the most superficial section of the two. It shows the constitution of the seventh and fifth nerves, and of the intestinal branch of the vagus. The anterior branch of the seventh nerve deserves a special notice.

Fig. 15 *b* mainly illustrates the dorsal commissure of the vagus nerve (*com*) continuous with the dorsal commissures of the posterior root of the spinal nerves.

Fig. 16. Two longitudinal and vertical sections of the head of a Pristiurus embryo belonging to stage K. Zeiss a, ocul. 1.

Fig. 16 *a* passes through the median line of the brain and shows the infundibulum, notochord and pituitary body, etc.

The pituitary body still opens into the mouth, though the septum between the mouth and the throat is broken through.

Fig. 16 *b* is a more superficial section showing the head cavities *pp.* 1, 2, 3, and the lower vagus commissure.

EXPLANATION OF PLATE XVIII.

Complete list of references.

cer. cerebral hemispheres. *ch.* notochord.
l v. lateral ventricle. *p cl.* posterior clinoid.
pn. pineal gland. *mn.* mandible.
x. rudiment of septum which will grow backwards and divide the unpaired cerebral rudiment into the two hemispheres.
c in. internal carotid. *op. n.* optic nerve.
op. eye. *in.* infundibulum. *pt.* pituitary body.
ol. olfactory pit. *ol. l.* olfactory lobe.
op. th. optic thalamus. *p c.* posterior commissure.

m b. mid-brain, or optic lobes. *cb.* cerebellum.
md. medulla oblongata. iv. *v.* fourth ventricle.
f t. fasciculi teretes. *r t.* restiform tracts.
t v. tela vasculosa of the roof of the fourth ventricle.
au. v. auditory vesicle. vii. seventh nerve.

Fig. 1 *a*, 1 *b*, 1 *c*. Longitudinal sections of the brain of a Scyllium embryo belonging to stage L. Zeiss a, ocul. 1.

1 *a* is taken slightly to one side of the middle line, and shows the general features of the brain, and more especially the infundibulum (*in.*) and pituitary body (*pt*).

1 *b* is through the median line of the pineal gland.

1 *c* is through the median line of the base of the brain, and shows the notochord (*ch.*) and pituitary body (*pt*); the latter still communicating with the mouth. It also shows the wide opening into the infundibulum in the middle line of the base of the brain.

Fig. 2. Section through the unpaired cerebral rudiment during stage O, to show the origin of the olfactory lobe and the olfactory nerve. The latter is seen to divide into numerous branches, one of which passes into each Schneiderian fold. At its origin are numerous ganglion cells represented by dots. Zeiss a, ocul. 2.

Fig. 3. Horizontal section through the three lobes of the brain during stage O. Zeiss a, ocul. 2.

The figure shows (1) the very slight indications which have appeared by this stage of an ingrowth to divide the cerebral rudiment into two lobes, *x*. (2) The optic thalami united by a posterior commissure, and on one side joining the base of the mid-brain. (3) The thin posterior wall of the cerebral rudiment with folds projecting into the cerebral cavity.

Fig. 4 *a*, 4 *b*, 4 *c*. Views from the side, from above, and from below, of a brain of Scyllium canicula during stage P, dissected out. In the view from the side the eye (*op.*) has not been removed.

The bilobed appearance both of the mid-brain and cerebellum should be noticed.

Fig. 5. Longitudinal section of a brain of Scyllium canicula during stage P. Zeiss a, ocul. 2.

There should be noticed (1) the increase in the flexure of the brain, accompanying a rectification of the cranial axis; (2) the elongated pineal gland, and (3) the structure of the optic thalamus.

Fig. 6 *a*, 6 *b*, 6 *c*. Views from the side, from above, and from below, of a brain of Scyllium stellare during a slightly later stage than Q.

Fig. 7 *a* and 7 *b*. Two longitudinal sections through the brain of an embryo during stage Q. Zeiss a, ocul. 2.

7 *a* cuts the hind part of the brain nearly in the middle line; while 7 *b* cuts the cerebral hemispheres and pineal gland in the middle.

In 7 *a* the infundibulum (1), cerebellum (2), the passage of the restiform tracts (*r t*) into the cerebellum (3), and the rudiments of the tela vasculosa (4) are shown. In 7 *b* the septum between the two lobes of the cerebral hemispheres (1), the pineal gland (2), and the relations of the optic thalami (3) are shown.

Fig. 8 *a*, 8 *b*, 8 *c*, 8 *d*. Four transverse sections of the brain of an embryo slightly older than Q. Zeiss a, ocul. 1.

8 *a* passes through the cerebral hemispheres at their junction with the olfactory lobes. On the right side is seen the olfactory nerve coming off

from the olfactory lobe. At the dorsal side of the hemispheres is seen the pineal gland.

8 *b* passes through the mid-brain now slightly bilobed, and the opening into the infundibulum (*in*). At the base of the section are seen the optic nerves and their chiasma.

8 *c* passes through the opening from the ventricle of the mid-brain into that of the cerebellum. Below the optic lobes is seen the infundibulum.

8 *d* passes through the front end of the medulla, and shows the roots of the seventh pair of nerves, and the overlapping of the medulla by the cerebellum.

EXPLANATION OF PLATE XIX.

Complete list of references.

v. fifth nerve.
v. *op. th.* ramus ophthalmicus of fifth nerve.
v. *mx.* „ maxillæ superioris of fifth nerve.
v. *mn.* „ mandibularis of fifth nerve.
vii. seventh nerve.
vii. *mn.* mandibular (spiracular) branch of seventh nerve.
vii. *hy.* hyoid branch of seventh nerve.
vii *a.* anterior branch of seventh nerve.
gl. glossopharyngeal nerve. *vg.* vagus nerve.
vg. r. roots of vagus nerves in the brain.
vg. com. commissure uniting the roots of the vagus, and continuous with commissure uniting the posterior roots of the spinal nerves.
vg. in. intestinal branch of vagus.
vg. br. branchial branch of vagus.
n l. nervus lateralis. *p r.* posterior root of spinal nerve.
a r. anterior root of spinal nerve. *v c.* visceral cleft.
sp. spiracle. *au. v.* auditory vesicle. *op.* eye.
ol. olfactory pit. *cer.* cerebrum. *ch.* notochord.
p ch. parachordal cartilage. *l l.* lateral line.
pp. head cavity. *hy. m.* hyaloid membrane.
p fal. processus falciformis. *rt.* retina.
ch. epithelial layer of choroid membrane. *v h.* vitreous humour.

Fig. 1. Diagram of cranial nerves at stage L.

A description of the part of this referring to the vagus and glossopharyngeal nerves is given at p. 468. It should be noticed that there are only five strands indicated as springing from the spinal cord to form the vagus and glossopharyngeal nerves. It is however probable that there are even from the first a greater number of strands than this.

Fig. 2. Section through the hinder part of the medulla oblongata, stage between K and L. Zeiss A, ocul. 2.

It shows (1) The vagus commissure with branches on one side from the medulla. (2) The intestinal branch of the vagus giving off a nerve to the lateral line.

Fig. 3. Longitudinal and vertical section through the head of a Scyllium embryo of stage L. Zeiss a, ocul. 2.

It shows the course of the anterior branch of the seventh nerve (vii.); especially with relation to the ophthalmic branch of the fifth nerve (v. *op. th.*).

Fig. 4 *a* and 4 *b*. Two horizontal and longitudinal sections through the head of a Scyllium embryo belonging to stage O. Zeiss a, ocul. 2.

4 *a* is the most dorsal of the two sections, and shows the course of the anterior branch of the seventh nerve above the eye.

4 *b* is a slightly more ventral section, and shows the course of the fifth nerve.

Fig. 5. Longitudinal and horizontal section through the hind-brain at stage O, showing the roots of the vagus and glossopharyngeal nerves in the brain. Zeiss B, ocul. 2.

There appears to be one root in the brain for the glossopharyngeal, and at least six for the vagus. The fibres from the roots divide in many cases into two bundles before leaving the brain. Swellings of the brain towards the interior of the fourth ventricle are in connection with the first five roots of the vagus, and the glossopharyngeal root; and a swelling is also intercalated between the first vagus root and the glossopharyngeal root.

Fig. 6. Horizontal section through a part of the choroid slit at stage P. Zeiss B, ocul. 2.

The figure shows the rudimentary processus falciformis (*p. fal.*) giving origin to the vitreous humour, and the hyaloid membrane (*hy. m.*) which is seen to adhere to the retina, and not to the vitreous humour or processus falciformis.

ON THE EARLY STAGES OF DEVELOPMENT OF THE NERVES IN BIRDS. BY A. MILNES MARSHALL, B.A., B.Sc. (Plates XX. and XXI.)[1]

(From the Zoological Laboratory, Cambridge.)

IN the investigations here recorded, which are concerned almost exclusively with the early stages of development of the nerves, chick embryos, incubated by the hen, and of ages varying from 36 hours to 4 days, were employed. These were hardened by immersion in picric acid—prepared after Kleinenberg's method—for 3 to 5 hours; and then transferred to alcohol of about 30 p. c., which was gradually increased in strength till absolute. As a staining agent Kleinenberg's preparation of hæmatoxylin was used.

Some specimens were hardened in chromic acid in the usual manner; but these have not proved nearly so satisfactory as picric acid specimens, and have only been used to confirm and control the results obtained from the latter: in fact, it is to the use of picric acid, as a hardening agent, that the results obtained are believed to be in great measure due. Very good results were obtained from duck-embryos, hardened in picric acid.

My observations, though I believe differing widely from any previous account of the chick, will be found to agree remarkably closely with Balfour's researches on the mode of development of the nerves in Elasmobranchs[2]. I mention this at once, as I shall have occasion to refer repeatedly to Balfour's paper.

Owing to the absence of protovertebræ, and to the mesoblast being less compact in the head, the early stages of development of the cranial nerves are more easily studied than those of the spinal, and will therefore be considered first.

Plate XX. fig. 1, represents a transverse section through

[1] An abstract of this paper was read before the Royal Society on March 8th.
[2] *Phil. Trans.* Vol. CLXVI. Pt. 1.

the hind-brain of a 43 hours chick. The exact position of the section can be defined, since it passes above through the deepest portion of the commencing auditory involution, *aud.*; while below it passes through the posterior part of the heart, only a short distance in front of the point of union of the omphalomeseraic veins.

The external epiblast, *ep.*, is seen to be very thin over the summit of the neural canal, where it consists of a single layer of somewhat flattened cells. Towards the sides it thickens rapidly, and is pushed in slightly from the exterior so as to form on either side a shallow depression lined by a thick layer of epiblast, of which the cells are elongated vertically, and arranged in one layer at the margin of the depression, but towards the centre in two or three layers. This depression, *aud.*, is the commencing auditory involution, which at this period has the form of a wide shallow pit, through the deepest portion of which, as noticed above, the section passes.

This layer of epiblast is seen to lie in close contact with the walls of the neural canal for some distance on either side; while between the top of the neural canal and the epiblast there is a considerable interval.

The hind-brain at this period is of considerable length, and presents three or more dilatations separated by slight constrictions. The section figured passes through the second of these dilatations a little way behind its centre. In section the brain at this point is seen to be nearly circular in outline; and the central canal, which is of considerable size, is also approximately circular. The walls of the canal are thicker at the sides than at the top or bottom, and consist of elongated cells arranged radially, and placed three or four deep. At the extreme summit of the canal, however, the cells are seen to alter their shape, becoming slightly smaller, and nearly circular in outline. These spherical cells grow upwards, and spread out on either side, forming a mass, *m.*, which occupies the interval above alluded to, between the top of the canal and the external epiblast.

This mass consists throughout of cells identical with those at the extreme summit of the cord, and differing markedly by their smaller size and more spherical shape both from the cells

composing the rest of the brain-wall, and from the superficial epiblast-cells.

As is evident from the figure, there are no mesoblast-cells anywhere near from which the mass (*m*) could possibly be derived, owing to the superficial epiblast being in contact with the sides of the brain for a considerable distance on either side. Moreover, we shall see that the cells of the mass differ in appearance very much from mesoblast-cells; while, finally, an examination of sections taken in parts where the mass (*m*) is much smaller, demonstrates conclusively that the cells composing it do really arise in the manner described above, *i.e.* as outgrowths from the extreme summit of the neural canal. This outgrowth forms the earliest stage in the development of the cranial nerves; and the stage here represented may well be compared with Balfour's figures, *op. cit.* Pl. XVI. B. 2 and 3.

Pl. XX. fig. 2, represents a section from the same embryo, taken a little further forward than fig. 1. It passes through the anterior edge of the auditory depression, which is hardly recognizable in the section, except by the thickening of the epiblast at the sides of the neural canal.

The mass (*m*) is somewhat larger than in fig. 1, and has grown outwards so as to form on either side an oval mass which indents the upper wall of the hind-brain; this indentation is visible in fig. 1, but is a much more prominent feature in fig. 2; it has the effect of causing the general contour of the brain together with the outgrowing mass to appear tolerably uniform, so that in imperfectly preserved specimens the presence of the outgrowth might easily be overlooked.

The outgrowths (*m*) are still connected with the extreme summit of the brain, though the connection is somewhat narrower than in the preceding stage. The outgrowths of the two sides are manifestly continuous with one another across the top of the neural canal.

The cells composing the outgrowths have not altered in appearance. Owing partly to their increased lateral extension, and partly to the alteration in contour of the external epiblast, due to the slight development of the auditory depression, the outgrowths lie very close to the mesoblast. It is now seen that the mesoblast-cells are larger than the cells forming the out-

growths, from which they differ also in being more loosely arranged, very irregular in shape and size, and in almost invariably giving out one or more processes, often of considerable length.

The neural canal has altered its shape: instead of being circular it is now somewhat oval, with the long diameter vertical: this change is still more marked in the next figure.

Pl. XX. fig. 3, is drawn from a section taken a very short distance in front of that represented in fig. 2, only two thin sections intervening. In it the outgrowths (*m*) have become much larger, and have grown downwards considerably on either side. Partly in consequence of this downgrowth, and partly owing to the external epiblast presenting only very slight lateral thickenings, the outgrowth on either side is in very extensive contact at its distal end with the mesoblast-cells: the two forms of cells are seen to differ widely from one another in the manner just noticed.

The outgrowths are still attached to the brain at its extreme summit only[1], and those of the two sides are still widely continuous with one another across the top of the neural canal.

Some of the cells of the outgrowth are seen to have altered their shape slightly, becoming oval instead of circular in outline.

Between figs. 1 and 2 four sections intervene, all showing the outgrowth (*m*), which is found to increase in size as we pass forwards from fig. 1 till we get to fig. 3, where it attains its maximum. In front of fig. 3 it rapidly gets smaller and almost completely disappears. At about the middle of the most anterior of the dilatations presented by the hind-brain, the outgrowth again becomes prominent, but assumes a slightly different form, shown in Pl. XX. fig. 4. In this figure the superficial epiblast is seen to be very thin in its whole extent, but is still thinnest over the summit of the canal. The hind-brain (*hb*) is considerably larger than it was further back: the outgrowth of spherical cells from its summit occurs in the same manner as it did in fig. 3: the lateral processes (*m*) are, however, much more slender, and have grown much further down than in fig. 3. The mesoblast-cells present the same characters

[1] The morphological importance of this attachment is very clearly stated by Balfour, *loc. cit.* p. 191.

as they did further back; but have grown round so as to lie between the outgrowth (*m*) and the superficial epiblast.

An examination of the sections immediately behind that represented in fig. 1, shows that the outgrowth (*m*) gets slightly smaller at first, then begins to dilate again, getting more and more prominent, till finally it attains the form shown in Pl. xx. fig. 5. This section, which passes below through the anterior part of the mid-gut, is completely behind the auditory depression: the external epiblast is seen to be thin in its whole extent, but especially so over the summit of the neural canal, which is oval in section and smaller than in the preceding figures. The outgrowth (*m*) is very prominent, and extends outwards some distance on either side; its limits are very sharply defined, though peripherally it is in extensive contact with the surrounding mesoblast-cells. The section passes through the most anterior proto-vertebra; and it is with the part of the muscle-plate (*mp*) nearest the neural canal that the outgrowth (*m*) comes in contact. The cells of the muscle-plate are elongated and fusiform, and differ widely from those of the outgrowth; which latter has a tendency to grow out horizontally so as to lie between the muscle-plate and the superficial epiblast.

We thus see that towards the latter part of the second day the cells along the median dorsal line of the hind-brain become slightly smaller and more spherical than those making up the rest of the wall of the neural canal; and that these spherical cells grow upwards, so as to form a prominent outgrowth immediately beneath the external epiblast, and between it and the top of the brain. Since this outgrowth is visible in some form or other in all the sections taken through the hind-brain, it follows that it is a continuous growth, in the form of a longitudinal ridge extending the whole length of the hind-brain. This ridge is more prominent at the posterior part of the hind-brain than it is anteriorly, where it gradually decreases in size and disappears[1]. At intervals along its length the ridge

[1] I have not always been able to detect an actual outgrowth in *all* the sections between the points indicated by Plate xx. figs. 3, 4; as the brain in this situation lies exceedingly close to the external epiblast. The cells along the

becomes more prominent, growing out into paired lateral processes. These processes are found, by a study of their later stages of development, to be the earliest rudiments of the cranial nerves.

Of those already described, the prominent outgrowth (*m*), seen in Pl. xx. fig. 3, is the commencement of the facial and auditory nerves.

The outgrowth shown in fig. 4 is the fifth nerve; which, though longer than the preceding, is at this period much more slender.

Behind the ear we have a conspicuous outgrowth of considerable length, which gradually increases in prominence from before backwards, and attains its maximum in Pl. xx. fig. 5. This subsequently gives origin to the glossopharyngeal and vagus nerves, and may be spoken of as the vagus-mass.

The sections posterior to that represented in fig. 5 show that the longitudinal ridge just described is not confined to the hind-brain, but extends backwards without any break for a certain distance down the spinal cord. As was the case in the brain, this ridge gives off at intervals paired processes, which grow outwards from the summit of the cord. These intervals correspond in number with the protovertebræ, and the processes themselves we shall find develope into the posterior roots and ganglia of the spinal nerves.

Pl. xx. fig. 6, represents a transverse section through the posterior part of the most anterior protovertebra of the same embryo, from which figs. 1—5 were taken; the section passing through one of the posterior roots (*m*). The external epiblast (*ep*) is very thin: the spinal cord presents in section a characteristic oval shape. The cells at the top of the cord become, as was the case in the brain, somewhat smaller and more spherical, and grow outwards on either side into a long slender process. Though this process comes in contact with the mesoblast-cells of the protovertebræ, yet its outline is sharp and definite, and there is at this stage not the slightest difficulty in determining the limits of the outgrowth, or whether any given cell belongs to the nerve-root or to the mesoblast.

median dorsal line have however the characteristic spherical shape in all the sections.

The nerve-root (*m*) lies on either side close beneath the external epiblast: its distal end lies *outside* the muscle-plate, between it and the external epiblast. This relation, which is shown to a slighter extent, as regards the vagus, in Pl. xx, fig. 5, is a characteristic feature of the upper (cervical) spinal nerves, and will be referred to again further on.

It is also seen that the nerve-root is larger on one side than on the other; and that the side on which it is larger is that on which the muscle-plate is less developed. The section, in fact, passes on the left side through the hinder part of the muscle-plate, but on the right side passes almost exactly through the interval between the first and second protovertebræ. Horizontal sections also show that the posterior roots do not lie opposite the centres of the protovertebræ, but are at first situated opposite their posterior halves; while in the case of a few of the upper (cervical) spinal nerves they extend further back, so as to overlap the anterior parts of the succeeding protovertebræ. The length of attachment to the cord of the posterior root of each spinal nerve is at first equal to about half a protovertebra.

The development of the posterior roots of the spinal nerves in the hinder part of the body resembles that just described as occurring in the anterior portion in its more important points, but presents some minor differences. The nerve rudiments are from the first much more slender than is the case further forwards. The spinal cord lies very close underneath the superficial epiblast, and, though the cells at the summit of the cord are always more spherical than the rest, I have not been able to satisfy myself of the presence of a continuous outgrowth, but am inclined to think that the nerves arise in pairs direct from the cord itself. The longitudinal extent of the attachments of the roots to the cord also seems to be less in the posterior spinal nerves.

Pl. xx. fig. 7, represents a transverse section through the dorsal region of a 3-day chick, and illustrates the next stage in the development of the posterior spinal roots. The spinal cord has, relatively to the muscle-plates, grown considerably, both laterally and vertically: owing to the vertical increase—which gives rise to a broad ridge along the back of the embryo—the position of the posterior roots has somewhat altered; instead of

projecting out laterally as they did in fig. 6, they now lie against the sides of the spinal cord: owing to this change in position their tendency to run outside the muscle-plates, noticed in the earlier stages, no longer exists. The nerve-roots are also seen to be much smaller relatively to the cord than in their earlier stages, which would obviously facilitate the change in their position.

Though unequal growth of the surrounding parts may possibly be sufficient to account for the change of position of the spinal nerves, I cannot regard it as satisfactory so far as the vagus is concerned, for, in one series of specimens, sections taken in the same position as that represented in Pl. XX. fig. 5, but at a rather later date, show that the tendency of the vagus to pass outside the muscle-plates is so decided that, in order to enable the nerve to subsequently pass inside the muscle-plate, some further explanation than a simple change in the relative rates of growth of different parts seems necessary: unless, indeed—and some of my specimens point very strongly to this conclusion—a part, at least, of the nerve remains permanently outside the muscle-plate, and just beneath the external epiblast.

The small size of the roots, (*m*) fig. 7, relatively to the spinal cord, is worth notice, as it shows that at this period the nerves grow relatively more slowly than the cord.

Another important feature is the point of attachment of the roots to the cord: this is no longer to the extreme summit, but to the angle between the top and sides of the cord; so that there is, at this stage, no evident outgrowth of cells from the summit of the cord. Later on we shall find the attachment shifting still further down the sides. The manner in which this change of attachment occurs is a matter of some uncertainty; but as far as the present stage is concerned, I am convinced that the explanation first proposed by Balfour[1] is correct, viz., that the shifting is apparent rather than real; and is due to rapid growth of the cells of the top of the cord, which would have the effect of separating the roots, and, as it were, forcing them further apart.

[1] *Loc. cit.* p. 182.

The last point to be noticed in fig. 7 is the appearance of a certain number of detached mesoblast-cells at the summit of the muscle-plate, and lying outside the nerve-root: these are shown on the right side only of the section: in appearance they do not differ much from the cells composing the nerve-root, from which however they may be distinguished by their more irregular shape, by their tendency to give out processes, and by their staining less deeply with hæmatoxylin.

The next stage is represented in Pl. xx. fig. 8, drawn from a section through the posterior dorsal region of a 4-day chick embryo. It differs from fig. 7 in several points, the more important of which are the following:—The slope of the back, due mainly to vertical increase of the spinal cord, is rather steeper. The posterior roots (*m*) are considerably larger, and have grown down on each side in close contact with the spinal cord, between it and the muscle-plates. The point of attachment of the roots is difficult to determine accurately; their upper or proximal parts are very slender, and in many cases it is impossible to trace any connection between them and the cord, against which they lie. The distal part of the nerve swells out considerably, forming an oval enlargement—the spinal ganglion (*g*). The section also shows that the ganglia do not lie opposite the centres of the muscle-plates, but almost opposite the intervals between successive pairs.

Another important point is the comparative difficulty now met with in distinguishing between the cells of the nerve-root and the adjacent mesoblast-cells. Many of the cells of the nerve and ganglion are no longer spherical, but more or less elongated; while the mesoblast-cells are slightly smaller, and much more closely packed together than they were at first; while many of them no longer give out processes, but are spherical or fusiform in shape, and almost indistinguishable from some of the cells of the nerve-root. The mesoblast-cells have also grown all round the top of the spinal cord, forming a distinct layer between it and the external epiblast; while some of them have grown in between the sides of the spinal cord and the nerve-roots. Consequently, while the limits of the nerve-roots were perfectly easy to define in the early stages, even when there was extensive contact between them and the meso-

blast-cells; in the later stages the exact limits become very difficult, or even impossible, to fix, and certain cells near the periphery of the nerve-root, especially those near its distal end, might be epiblast-cells belonging to the root, or mesoblast-cells. It follows therefore that while it appeared certain that the growth of the nerve in its earlier stages was effected by multiplication of the cells of the original outgrowth, and consequently of epiblastic origin; in the later stages it is impossible to determine whether the nerve can still be described as a structure of purely epiblastic origin, or whether its growth is due in part to conversion of the adjacent mesoblast-cells.

With the structure of the spinal cord we are not directly concerned, but the presence of large numbers of spherical, or nearly spherical, cells in its substance is shown in the figure.

To recapitulate. The longitudinal ridge described in the hind-brain, as formed by an outgrowth of cells from the extreme summit of the neural canal, is continued down the spinal cord for a certain distance, but becomes inconspicuous in the hinder part of the body, where its presence has not been definitely ascertained. We find further that this ridge gives off paired processes opposite the posterior half of each protovertebra, these processes being the rudiments of the posterior roots of the spinal nerves: that these processes at first grow outwards just beneath the external epiblast; but subsequently, owing to changes in the shape of the embryo caused by unequal growth of different parts, alter their direction somewhat, and pass downwards between the muscle-plates and the spinal cord: that the proximal portion of each process becomes more slender, and that its point of attachment to the cord shifts outwards somewhat: that the distal portion of the process enlarges considerably, and becomes a spinal ganglion: finally, that these processes originally consist throughout of spherical nucleated cells, differing widely in appearance from the adjacent mesoblast-cells; but that, in the course of development, many of these cells become elongated and fibrillar, and that the distinction between the cells of the nerve and the mesoblast-cells becomes much less evident.

Hitherto all accounts of the development of the nerves in the chick, with the single exception of that given by His, agree in stating that the nerves, both cranial and spinal, arise in the mesoblast, and acquire their connection with the neural canal by a subsequent growth inwards[1].

His however has given a very different account[2], which may be briefly summarized thus:—according to him the first stage in the development of the posterior roots consists in the appearance of downgrowths of the external epiblast on either side of the summit of the spinal cord: these downgrowths are more strongly marked at intervals corresponding in number to the muscle-plates: they then separate from the external epiblast and form groups of cells, triangular in transverse section, situated between the spinal cord on the inner side, the protovertebra on the outer side, and the external epiblast above. These groups of cells develope into the spinal ganglia: they develope processes inwards to join the spinal cord, and outwards to form the part of the nerves beyond the ganglia.

The above description agrees with mine, and differs from the usual accounts (1) in assigning an epiblastic instead of a mesoblastic origin to the nerves: (2) in describing the nerves of the body as arising perfectly independently of the protovertebræ, instead of from parts of them. We also agree in describing the cranial nerves as arising in the same manner as the posterior roots of the spinal nerves.

My observations however lead me to differ from His on the following points:—(1) I find the nerves arise as outgrowths from the neural canal instead of from the external epiblast; (2) I do not find the ganglion to be the first part developed. Other differences, such as the development of the continuous longitudinal ridge, of which His omits all notice, readily suggest themselves: but the two just mentioned seem to me to be the most fundamental.

I have found that opposite the centre of each protovertebra the external epiblast does really grow downwards as a conical process on either side of, and in close contact with, the neural canal. From comparison with His' figures and descriptions,

[1] Foster and Balfour, *Elements of Embryology*, Pt. I. pp. 151, 152.
[2] *Die erste Anlage des Wirbelthierleibes.* Leipzig, 1868.

there is no doubt that these processes are the same that he describes: they are well marked in the body, especially in its hinder part, but are only very slightly developed in the head: they are of very slight longitudinal extent, and differ widely in appearance from the nerve-roots, with which I am perfectly satisfied they have no connection whatever, except that of simple apposition.

His gives several figures showing different stages in the development of the nerves, both cranial and spinal. From a careful examination of these figures and the descriptions given by His and by comparing them with my own specimens, I am convinced that His really saw the early stages of development, but was led into error as to their nature by imperfectly prepared specimens. He makes no attempt to represent the histological details of his sections, which we have seen to be of great importance in studying the early stages.

His figures two sections[1] through the hind-brain of a 38-hours chick, in both of which there is a large mass of cells on the summit of the brain between it and the external epiblast. The figures, it is true, show no connection between this mass and the brain, but neither do they show any between the mass and the external epiblast. The mass in fig. 3 corresponds exceedingly closely in appearance and position with the outgrowth (*m*), fig. 3, Pl. XX, and is unquestionably the same structure. The mass in the other section, which is described as passing through the mid-brain, but which I believe to pass through the anterior part of the hind-brain, is somewhat smaller, and closely resembles that which I have figured in Pl. XX. fig. 1.

Though therefore I differ from His on several fundamental points, I can appeal confidently to these two figures as confirming my statements, as far as the position and general appearance of the outgrowths are concerned, at the period mentioned.

His commenced by studying the spinal nerves, where he was misled by the downgrowths of the external epiblast. Had he commenced with the cranial nerves he could hardly have fallen

[1] *Op. cit.* Taf. VII. fig. 2, 3.

into this mistake, as, according to his own figures, the down-growths of epiblast in the head are very slightly developed.

It is important to notice that His suggests that the portion of nerve connecting the spinal ganglion (which he wrongly supposes to be the earliest developed part of the nerve) with the cord may possibly be an outgrowth from the cord, and not from the ganglion: he decides however in favour of the latter view.

Though the results of my observations thus differ widely from any previously published account of the chick with which I am acquainted, they will be found to agree remarkably closely with the account given by Balfour[1] of the development of the nerves in Elasmobranchs, which they serve to confirm in several of the most important points. This agreement refers not only to the general features, but even to the minute histological details. I have already had occasion to notice some of the points of this agreement: but in order to appreciate it fully, it is necessary to compare his figures and descriptions with those given here. Since an account of Balfour's researches, which have been extended considerably since the publication of the paper above referred to, appears in the present number of this Journal, I may refer the reader to his own paper for the detailed description.

Hensen[2] has described and figured the posterior roots of the spinal nerves as arising in the rabbit as direct outgrowths from the summit of the spinal cord: his figures correspond fairly closely with that given in Plate XX. fig. 7. As regards the chick however, his own observations, strangely enough, lead him to adopt the same view as His, viz. that they are developed from the deeper layer of the external epiblast.

A mode of development of the nerves that is common to a group of vertebrates with very generalized affinities, Elasmobranchs (Balfour), and to two highly specialized groups, Mammals (Hensen) and Birds, may fairly be assumed to be typical of the sub-kingdom, and will probably prove to be the actual mode of development in other vertebrate groups besides those mentioned[3].

[1] *Op. cit.*
[2] *Zeitschrift f. Anatomie u. Entwickelungsgeschichte*, 1876. Bd. 1.
[3] Since writing the above I have satisfied myself that the description just given of the development of the nerves in the chick will apply also to the cranial

I have not yet determined the exact date of the earliest appearance of the nerves: in a chick of 43 hours we have seen the rudiments of the most important cranial nerves already established, as well as the posterior roots of the first six or more spinal nerves. I have not yet made satisfactory preparations of younger specimens showing the nerves, but judging from the rate of growth afterwards, we cannot be far wrong in assigning a period a little before the middle of the second day as the time of the first appearance of the nerve-rudiments.

The spinal nerves are developed in succession from before backwards: while, judging from the figures given by His, the cranial nerves appear first of all.

The anterior roots of the spinal nerves are not easy to investigate. My observations on their development are not so complete as I could wish, but, as far as they go, accord fairly well with those of Balfour on the Elasmobranchs.

They appear later than the posterior roots, a fact recognized by His, arising as outgrowths from the lower part of the sides of the spinal cord.

In Plate XX. fig. 8, it will be noticed that the superficial cells of the lower part of the cord converge slightly towards a point (*a*); this is the spot at which the anterior root will shortly be developed; and this convergence is usually recognizable a short time before the actual appearance of the root.

The next stage is shown in Plate XXI. fig. 10, a transverse section through the cervical region of a 4-day duck embryo, which shows the anterior roots as small processes projecting outwards from the spinal cord. The section is taken only a short distance behind the head, a region in which, owing to the mesoblast being less dense than it is further back, the early condition of the nerves is comparatively easy to study. Further back the mesoblast is very compact, vide Plate XX. fig. 8, and the anterior roots difficult to recognize, especially when small.

The outgrowth to form the anterior root (*a*) is very slender

nerves of the Tadpole; and, I have strong reasons for adding, to the nerves, both cranial and spinal, of the Salmon. My observations in Salmon-embryos are, however, very imperfect as yet.

at its origin, and is at first directed outwards and somewhat upwards: it then turns downwards at an open angle, at the same time enlarging somewhat, though still remaining much more slender than the posterior root. It consists from the first of elongated fusiform cells, except at the attachment to the cord, where some of the cells are small and spherical.

Horizontal sections show that each anterior root at a very early stage consists of a series of small outgrowths placed one in front of another and converging slightly as they pass outwards into the mesoblast. Each anterior root has, about the 75th hour, a longitudinal extension equal to about half a protovertebra, opposite the anterior half of which it is at first situated; the posterior roots being at this period about opposite the intervals between successive protovertebræ. I have not been able to determine whether each anterior root arises originally as a single outgrowth, or whether it consists from the first of a series of outgrowths. These stages are difficult to investigate owing to the exceedingly slender attachment of the anterior roots to the spinal cord. The origin of the anterior roots by several processes is a point in which the chick differs from Elasmobranchs.

In Plate XXI. fig. 10, the posterior roots (*p*) are seen in section, but not their points of attachment to the cord.

The last stage with regard to the spinal nerves which I propose to consider in the present paper is shown in Plate XXI. fig. 9, which represents a transverse section through the anterior dorsal region of a 75-hour chick, passing through both anterior and posterior roots. The anterior have grown out to meet the posterior roots and so form the spinal nerves, which run downwards on the inner side of the muscle-plate.

The posterior root is seen to be attached on the left side by a small pedicle to the upper part of the side of the cord: on the right side the section has just missed the point of attachment. It will be noticed that this point of attachment of the posterior root is considerably lower than it was in Plate XX. figs. 7 and 8: a more important difference is that the nerve-root is no longer attached by its extremity to the cord, but forms a considerable swelling above this point of attachment.

We have already seen a tendency on the part of the roots to shift their attachments outwards: this is shown in fig. 7, and has been explained as due to rapid growth of the cells at the summit of the cord. This shifting may have increased so much as to cause the marked change in position seen in fig. 9; in which case the growth upwards of the nerve above the root would be a secondary change.

Another possible explanation is that the original attachment to the top of the cord has been completely lost, and a new one developed in the situation of the permanent posterior root: in this case the outgrowth above the point of attachment would simply be the remnant of the original root.

My preparations have not enabled me as yet to determine with certainty which of these explanations is the correct one; but the following facts seem to speak strongly in favour of the latter one. During the stage represented in fig. 8, it is exceedingly difficult to determine whether the posterior root is still attached to the cord or not; and it is only in occasional sections that I have been able to trace the connection. When the connection was demonstrated, it was, as shown in fig. 8, exceedingly slender. I have never observed specimens in which the nerve was attached at a point lower than that shown in fig. 7, yet above that in fig. 8. The outgrowth above the point of attachment rapidly becomes smaller, and is lost in specimens but little older than that in fig. 9: this transitory nature is readily comprehensible on the one hypothesis, but a serious difficulty on the other; as it would be very hard to understand why such an outgrowth should arise at such a stage in development, and disappear again so rapidly. The general lines of direction of the cells composing the cord, which are indicated in fig. 9, strongly favour the view that the permanent attachment is a secondary one, and not the original one altered in position; while at the same time they favour the view which regards the outgrowth above the point of attachment as a remnant of the primary root. Lastly, the cells composing this projection differ from the cells of which the rest of the root consists in being spherical or nearly so, while the rest of the root is made up of considerably elongated cells. This rounder form causes them to resemble the cells of the original out-

growth. However, as I have not yet traced all the stages I cannot consider the point as settled.

The outgrowth in question has been observed in Elasmobranchs by Balfour, who describes it thus[1]: "the proximal portion (of the nerve-rudiment) presents a fairly uniform diameter, and ends dorsally in a rounded expansion: it is attached remarkably enough, not by its extremity, but by its side, to the spinal cord." He however does not adopt the suggestion here made as to its origin and meaning, but considers it to be part of a dorsal longitudinal commissure he has detected connecting the posterior spinal roots together. I have failed to detect this commissure in the chick. Balfour's figures H. 1. and I. 1. correspond closely, as far as this outgrowth is concerned, with Pl. XXI. fig. 9.

The ganglion (*g*) is but slightly developed at this stage. The attachment of the anterior root to the cord is seen to be still very slender: the convergence of the cells of the cord to this point—indicated in the figure by the lines on the cord—is very well marked. Outside the cord the anterior root first passes outwards and upwards for a very short distance, dilating as it does so; it then bends rather sharply downwards, and, becoming considerably thicker, joins the posterior root and runs down on its inner side. The two roots can be readily distinguished from one another owing to the cells of the anterior root being very much more elongated than those of the posterior. The two roots run side by side for a short distance without blending, but further on become completely fused.

My study of the cranial nerves has been confined as yet entirely to the earlier stages; and even with regard to them my observations are very fragmentary and imperfect. Still some points of interest have presented themselves, to which I shall refer briefly.

We have seen that, towards the end of the second day, there is behind the auditory pit a continuous outgrowth from the summit of the hind-brain, of considerable longitudinal extent. This outgrowth is connected—by means of the longi-

[1] *Op. cit.* p. 185.

tudinal ridge so often alluded to—anteriorly with that from which the 7th and 8th nerves are derived, and posteriorly with that which gives origin to the posterior roots of the first pair of spinal nerves. From it the vagus and glossopharyngeal nerves are derived.

Though I have not worked out the later stages satisfactorily, the following points suggest themselves as worthy of notice. Firstly, the marked tendency of the vagus outgrowth to pass outside the muscle-plate between it and the superficial epiblast: this has been already noticed. Secondly, the fact that transverse sections through the hinder part of the vagus outgrowth pass also through the first protovertebra, vide fig. 5: in other words, that the vagus outgrowth, which is of considerable longitudinal extent, reaches backwards so as to overlap the anterior half of the first protovertebra. Thirdly, I would note as a point of some morphological interest the fact that the glossopharyngeal and the whole of the vagus arise at first as a *single continuous outgrowth*[1], from the distal edge of which the several branches are subsequently derived. If then the vagus is to be considered as equivalent to a number of spinal nerves fused together—a view in favour of which there is a considerable amount of evidence—this earliest condition of the vagus outgrowth may prove to be an indication that the fusion first occurred at a very early period in the phylogeny of the chick, and possibly in that of other vertebrates also.

I have no observations on the development of the spinal accessory and hypoglossal nerves; but the backward extension of the vagus outgrowth over the anterior protovertebra may help to render it intelligible how one or other of these nerves may appear in one group of vertebrates to be cranial, in another spinal.

Pl. XXI. fig. 12, represents a longitudinal section through the head and neck of a 4-day duck embryo; passing through the mid-brain (*mb*), hind-brain (*hb*), and anterior part of the spinal cord (*s*). The section is slightly oblique, passing rather deeper on the left than the right side. On the right side one of the branches (*v*) of the vagus-outgrowth is seen cut transversely; on the left side at (*v'*) the section passes through the point of origin

[1] Vide also Foster and Balfour, *Elements of Embryology*, Part I. p. 138.

of the vagus outgrowth: at (*v*) on the same side a part of the vagus is seen in the form of a longitudinal rod; but whether this corresponds to the commissure described by Balfour[1] as connecting all the roots of the vagus in Elasmobranchs, I have not determined. At *p*. are seen sections of the posterior roots of a spinal nerve.

Immediately in front of the auditory involution a single large root arises on each side, from which both the auditory and facial nerves are derived. This is represented in transverse section in Pl. XX. fig. 3; and in horizontal section in Pl. XXI. fig. 11, which is a horizontal section through the neck and hind-brain of a 75-hours chick. A large nerve, (*b*) fig. 11, is seen arising on each side from the second of the dilatations of which the hind-brain consists: it runs backwards and expands considerably, forming a large mass closely applied to the anterior wall of the auditory vesicle (*aud*).

In Pl. XXI. fig. 12, the facial nerve (*f*)—which is derived from the anterior part of the outgrowth common to it and the auditory nerve—is seen passing down in front of the auditory vesicle, from which it is quite distinct. On the right side of the section, which, as just noticed, is at a deeper level than the left, and passes below the auditory vesicle, the facial nerve (*f*) is still seen, but lies somewhat further back than it did on the left side, showing that it grows at first downwards and slightly backwards.

The 5th nerve has already been seen in transverse section in Pl. XX. fig. 4, arising as an outgrowth of very slight vertical thickness from the summit of the anterior dilatation of the hind-brain. In Pl. XXI. fig. 12 *t*, it is shown in horizontal section at a somewhat later stage.

The root is seen to have a considerable longitudinal extension now; and transverse sections at this period show that the vertical extension has also increased. The point of attachment has shifted down from the extreme summit of the brain, and is situated some distance lower down. The nerve runs outwards, increasing considerably in width, and divides distally into two branches, an anterior smaller and a posterior larger one. These

[1] A Preliminary account of the Development of Elasmobranch Fishes. *Quart. Journ. Micros. Science*, 1874. Plate XV. fig. 14. *v.g*.

two branches I have been able to identify with the two described by Foster and Balfour as existing at the end of the third day[1]. Though the 5th nerve arises as a single outgrowth on either side, yet the condition of the vagus and glossopharyngeal in their earliest stages must render us very cautious about inferring that it therefore corresponds to a single spinal nerve.

Figs. 11 and 12 show that the so-called "hind-brain" does not consist of a single vesicle, but of a series of dilatations, separated by slight constrictions, and gradually decreasing in size from before backwards. Of these the most anterior and largest one, which at the end of the second day is but little smaller than the mid-brain, gives origin at its widest part to the 5th nerve. This relation I have found to occur invariably in all embryos up to the end of the fourth day that show any trace of a 5th nerve: it confers a considerable amount of constancy on this dilatation[2].

From the second dilatation the combined root of the 7th and 8th nerves arises. I am not however satisfied that this relation is invariable. The succeeding dilatations are much smaller and closer together, and do not appear to be constant in number or relations.

Not only does the whole "hind-brain" consist of a series of these dilatations, but the spinal cord also presents a similar, though less strongly marked, series; being slightly constricted opposite the centre of each protovertebra, and dilated opposite the intervals between successive pairs.

At the 50th hour a small outgrowth from the mid-brain is visible on either side close to the median dorsal line; this grows rapidly, and by the end of the fourth day forms a nerve of considerable size running from the mid-brain to the posterior part of the eye, and lying at a rather deeper level than the anterior (or ophthalmic) branch of the 5th nerve, which it crosses almost at right angles. From its position and relation it can

[1] *Elements of Embryology*, Part I. pp. 137, 8, and fig. 40, p. 142.

[2] Foster and Balfour (*loc. cit.* p. 138) mention the series of dilatations as existing on the third day, and suggest that they "may perhaps be viewed as indications of an aborted segmentation of the hind-brain into a series of vesicles." It is therefore a matter of some importance to determine whether they possess any constancy in their relations.

only be the 3rd nerve, which is thus from the first perfectly independent of the 5th.

My observations on the development of the olfactory nerves have led to results which differ materially from the ordinarily received accounts. According to Foster and Balfour[1] an "olfactory vesicle" grows out from the under surface of the cerebral hemisphere of either side towards the end of the third day; while the superficial epiblast is driven in to form a nasal pit. The pit and vesicle are not connected at first. This connection is generally described as brought about by the development of an olfactory nerve in the mesoblast, between the vesicle and pit. My own observations lead me to the conclusion that the olfactory nerves really arise as solid outgrowths from the anterior part of the fore-brain, near the median dorsal line.

Pl. XXI. fig. 13, represents about half of a section taken through the fore part of the head of a 4-day duck embryo in a plane transverse to the longitudinal axis of the fore-brain. The figure is semi-diagrammatic, the mesoblast being entirely omitted and no attempt made to represent the histological details. The section passes through the olfactory depressions, of which that on one side only is shown. The external epiblast is seen to be very thin over the roof and floor of the fore-brain, but is thickened at the sides, and driven in so as to form a shallow pit—the olfactory pit or involution (*na*)—of which the thickened epiblastic lining will become the special olfactory epithelium. The fore-brain is approximately circular in section; its walls are rather thinner at the top and bottom than at the sides. The olfactory nerve (*olf*) is a short solid body stretching from the upper part of the fore-brain downwards and outwards to the upper part of the olfactory pit: it consists of elongated fusiform cells which are in intimate relation on the one hand with the walls of the fore-brain, and with the cells of the olfactory epithelium on the other. The actual connection of nerve and brain was not seen in the section figured, but in one a little further back.

The same structures are shown in another plane in Pl. XXI. fig. 14, which represents a horizontal section through the fore part of the head of a 75-hours chick, in a plane parallel to the

[1] *Loc. cit.* p. 117.

longitudinal axis of the fore-brain. If it is borne in mind that figs. 13 and 14 represent sections of the same parts taken in planes at right angles to one another, the relation of the parts will be readily understood. It will be seen that the section in fig. 14—which is not perfectly horizontal—passes through the olfactory pit on the left side, and on the right side just above it, so as to miss the pit, but cut the olfactory nerve (*olf*). The nerve is seen at this point to be quite distinct from the brain.

Fig. 15 is a section from the same embryo as fig. 14 and parallel to it, but in a slightly higher plane. On the left side the nerve has approached somewhat nearer the middle line, and lies very close to the brain, from which however it is still perfectly distinct. On the right side the section passes through the point at which the nerve is attached to the brain.

The condition of the fore-brain requires some notice, as I have found the ordinary accounts to be somewhat misleading. Fig. 14 shows that the fore-brain at 75 hours is considerably dilated in front of the optic vesicles, forming a large prominent swelling, which occupies the extreme front of the head, and is nearly circular in transverse section (fig. 13). The cerebral hemispheres appear first as dilatations of the sides and upper part of this expanded fore-brain, and when seen in horizontal section bear a very similar relation to the fore-brain that the commencing optic vesicles originally did (vide Pl. XXI. fig. 15. *ch*).

Of an olfactory vesicle there is no trace whatever in the early stages. The olfactory nerves at first arise from the fore-brain, and not from the cerebral hemispheres: this is shown very clearly in figs. 13, 14 and 15, from which we also see how the subsequent growth forwards of the cerebral hemispheres will cause the nerves to appear to spring from their under surface.

The appearance, position and relations of the olfactory nerves at the 75th hour so closely resemble those of the other cranial nerves described above, as to strongly suggest that they are strictly comparable; and that the olfactory nerves are really the first pair of true cranial nerves. More accurate observations than we appear to possess at present on the development of the olfactory nerves in less specialized vertebrates are, however, necessary before this point can be considered as established.

If the olfactory nerves really prove to be, as I have just suggested, the first pair of true cranial nerves, many of the theories propounded concerning the composition of the vertebrate head will require modification. I will only allude here to the value attached to the distribution of the cranial nerves by Prof. Huxley, who starts with the assumption that the 5th nerve is the most anterior of the true cranial nerves.

In conclusion, I would say a few words on the distinction between the head and body. Sections of the neural canal, whether transverse or horizontal, do not enable us to fix any point as a limit between brain and spinal cord. In different specimens the sections vary considerably in appearance: in some the characteristic oval section of the cord—as seen in Pl. xx. fig. 6—is attained in parts that are unquestionably brain, while in others it is not acquired till the second protovertebra.

We have also seen that the outgrowths of cells from the summits of the brain and cord are perfectly continuous, and present no character that enables us to mark a limit between head and body.

The vagus-root has already been alluded to as overlapping the anterior half of the first protovertebra; and the close similarity in form between the vagus outgrowth and that for the spinal nerves has been pointed out.

Since then no definite indication of a limit between head and body is afforded by either the neural canal, the longitudinal outgrowths from its summit, or by the mode of development of the nerves, we must conclude that all these features were acquired before the distinction between head and body.

At the end of the second day the only means of fixing a limit is furnished by the protovertebræ; the anterior border of the first protovertebra marks the posterior border of the head. Here however we must bear in mind the fact that the anterior protovertebra is not the first to be developed[1].

Under these circumstances Balfour's failure to detect anterior roots to the cranial nerves of Elasmobranchs[2] becomes of special importance, as indicating the possible existence of a sharp distinction between head and body. I have not yet

[1] Foster and Balfour, *loc. cit.* p. 57.
[2] *Loc. cit.* p. 189, note.

detected anterior roots in the Bird in any sections taken in front of the first protovertebra; but, owing to the vagus-root overlapping the first protovertebra, I am by no means certain that the most forwardly situated of the anterior roots does not really belong to the vagus. Since however I have not examined embryos later than the end of the fourth day, and have not identified several of the cranial nerves at all, I cannot attach much importance to this failure, nor consider it as affording any decided confirmation of Balfour's observations just alluded to.

EXPLANATION OF THE FIGURES.

All the drawings were outlined with a Hartnack camera: the objective indicated as employed in each case is merely that used in drawing the outline: the details were filled in from a Hartnack obj. 8; oc. 3, and Zeiss obj. F; oc. 3.

Plate XX.

ep. external epiblast. *h.b.* hind-brain.
m. outgrowing mass from top of neural canal.
aud. auditory pit. *n.* notochord.
s. spinal cord. *m.p.* muscle-plate.
g. spinal ganglion.
a. position of anterior root of spinal nerve.

Figs. 1—6. Represent transverse sections from the same embryo—a 43-hours chick. Picric acid. Hartnack camera obj. 4.

Fig. 1. Section through hind-brain, passing through deepest portion of auditory pit (*aud.*).

Fig. 2. Through hind-brain, a short distance in front of fig. 1.

Fig. 3. A short distance in front of fig. 2: passes through common root (*m*) of 7th and 8th nerves.

Fig. 4. Section through the most anterior dilatation of the hind-brain, passing also through the 5th nerve (*m*).

Fig. 5. Section taken a short distance behind fig. 1; passing through the anterior part of the first protovertebra—(*mp*): and through the vagus-root (*m*).

Fig. 6. Through posterior part of first protovertebra: passing also through the first spinal nerve (*m*).

Fig. 7. Transverse section through the dorsal region of a 3-day chick. Hartnack camera obj. 4. Shows posterior spinal roots (*m*), and points of attachment to cord.

Fig. 8. Transverse section through the posterior dorsal region of a 4-day chick embryo. Hartnack camera obj. 4. Shows spinal ganglion (*g*) and point (*a*) at which the anterior root will shortly appear.

Plate XXI.

All the figures in this plate are semi-diagrammatical; no attempt having been made to represent the mesoblast or the histological details.

Fig. 9. Transverse section through the anterior dorsal region of a 75-hours chick, passing through both anterior and posterior spinal roots. Hartnack camera obj. 4.

s. spinal cord. *mp.* muscle-plate.
p. point of attachment of posterior root to cord.
g. ganglion. *a.* anterior spinal root.
n. notochord.

Fig. 10. Transverse section through the cervical region of a 4-day duck embryo, taken just behind the head. Hartnack camera obj. 2.

a. anterior spinal root. *p.* posterior spinal root.
n. notochord. *mp.* muscle-plate.

Fig. 11. Horizontal section through the hind-brain of a 75-hours chick. Hartnack camera obj. 2, reduced ⅔.

hb. cavity of hind-brain. *aud.* auditory vesicle.
b. root of 7th and 8th nerves. *n.* notochord.

Fig. 12. Horizontal section through head and neck of a 4-day duck embryo. Hartnack camera obj. 2, reduced ½.

mb. cavity of mid-brain. *hb.* cavity of hind-brain.
s. spinal cord. *mp.* muscle-plate.
t. root of 5th nerve. *f.* facial nerve.
aud. auditory vesicle. *v.* vagus.
v′. root of vagus. *p.* posterior roots of spinal nerves.

Fig. 13. Section through fore part of head of a 4-day duck embryo, in a plane transverse to the longitudinal axis of the fore brain. Hartnack camera obj. 2.

ep. external epiblast. *fb.* cavity of fore-brain.
na. nasal pit. *olf.* olfactory nerve.

Fig. 14. Horizontal section through fore part of head of a 75-hours chick embryo. Hartnack camera obj. 2, reduced ½.

fb. cavity of fore-brain. *na.* nasal pit.
olf. olfactory nerve.

Fig. 15. Section from same embryo as fig. 14, and parallel to it, but in a slightly higher plane. Hartnack camera obj. 2, reduced ½.

fb. cavity of fore-brain. *ch.* cerebral hemisphere.
olf. olfactory nerve. *ep.* external epiblast.

NOTE TO MR GUNN'S PAPER. P. 357.

The above observations were completed last June, and the paper was sent in (in August) for publication in the October number of this Journal. But from accidental causes the publication has unfortunately been deferred until now. In the interval, Prof. Fr. Merkel, of Rostock, has published, in the *Archiv. für Ophthalmologie*, observations which strikingly corroborate those made by Dr Gunn. This independent corroboration is of value, not only on account of Prof. Merkel's high reputation as a histologist, especially on the subject of the eye, but also from the fact that he has arrived at a similar conclusion by a different method of working—Dr Gunn's results having been obtained from the study of sections, Prof. Merkel's mainly from observation of the separated retinal elements.

E. A. SCHÄFER.

UNIVERSITY COLLEGE,
March, 1877.

EXPLANATION OF PLATE XII.

Fig. 1. Vertical section through Human Retina, *a.* cone, *b.* cone-nucleus, *c.* cone-fibre, *d.* cone-fibre enlargement or cone-bulb, *e.* bipolar inner "granule," its outer process extending to *d*, its inner becoming lost abruptly in the inner molecular layer, *f.* ganglion-cell, *a'.* rod, *b'.* rod-nucleus, *c'.* rod-fibre shewing minute varicosities, *d'.* rod-fibre enlargement or rod-bulb, *l. e.* membrana limitans externa; *M.* base of Müllerian fibre.

Fig. 2. Cone, cone-nucleus, cone-fibre and cone-bulb: to the latter an inner granule is seen to send a well-defined wavy process, while two neighbouring inner granules send processes towards, but not traceable into, the same cone-bulb.
m. external molecular layer.

Fig. 3. An apparent direct continuation of a branch of a ganglion cell (*f*) with the inner process of an internal granule (*e*): the outer process of this granule is prolonged into a cone-bulb (*d*): *e'.* an inner granule attached to an off-shoot of the same branch of the ganglion cell; another branch of the ganglion cell seems to go directly to an inner granule *e''*.

Fig. 4. Cone-bulb showing a connection with two inner granules: the process of one is short, broad and straight; that of the other, longer, narrow and wavy.

Fig. 5. Like the last, but the second wavy process is not traceable into the cone-bulb.

Fig. 6. The outer process of this inner granule (*e*) exhibits an enlargement about the middle of its course through the intergranular layer, from which proceed several minute branches, one entering the cone-bulb (*d*).

Fig. 7. The outer process of the inner granule (*e*) bifurcates in the substance of the intergranular layer. From one branch three very delicate twigs proceed directly towards three rod-bulbs (*d'*).

FURTHER OBSERVATIONS AND EXPERIMENTS REGARDING THE TRUE NATURE OF TETANUS.

By SYDNEY RINGER, M.D., *Professor of Therapeutics at University College,* and WILLIAM MURRELL, L.R.C.P., *Medical Registrar at Westminster Hospital.*

IN a paper published in the Medico-Chirurgical Transactions for 1876, we controverted the view commonly accepted that tetanus is always due to increased excitability of the spinal cord, and we detailed numerous experiments to prove that in tetanus the resistance of the cord is diminished or destroyed, so that an impression conveyed by an afferent nerve can spread throughout the reflex portion of the central nervous system and produce tetanus. Many persons having expressed strong doubt as to the existence of this "resistance," we propose now to give the reasons for our belief in this property, and to shew that it is not fixed, nor unmodifiable, but that probably disease, certainly some drugs, will weaken or destroy it, the other functions of the cord meanwhile remaining unimpaired or but slightly depressed.

We first draw attention to the fact that this resistance is recognised in recent works on Physiology. Thus Hermann says, resistance of the cord is lessened in tetanus, and Ferrier, that in strychnia tetanus "the resistance to radiation is diminished." This view, however, is more definitely and more cogently propounded by Dr Michael Foster, than by any other physiologist with whom we are acquainted. In his recent *Text Book of Physiology* he explains in the most luminous way the part which "resistance" plays in nervous phenomena[1].

[1] Whilst this paper is in the press, our attention has been called to Bernstein's *Nerven und Muskel-Systeme*, 1871. In Section IV. he arrives at very similar conclusions to those we have expressed in the paper already referred to. He says, "Physiological facts point to the conclusion that there is a connection of the sensory centres with one another," "for a phenomenon which forcibly points to such a connection, is that of irradiation. It is known that if a sensation is increased so as to become pain, it will not confine itself to the spot which has been irritated; the whole hand, nay, the whole arm, may ache, if the cause of the pain is only in a finger. It even happens that in such a case we feel the same sensation of pain in the corresponding finger of the other hand, though in a less degree. This phenomenon can only be explained by peculiar arrangements and processes in the perceiving central organs." "But it will be asked,

We were unaware till after writing our paper that this property of the cord was recognised; when, on referring to Hermann's *Physiology*, we found it mentioned there, and we adopted his expression "resistance" instead of the term "increased diffusibility" we had devised for ourselves.

Most writers consider tetanus to be due simply to increased excitability of the cord; indeed, in most works on Therapeutics it is taken for granted that tetanus is evidence of increased excitability of the cord.

Those writers who attribute tetanus simply to increased excitability of the cord imply the existence of resistance, though they do not appear to recognise the necessity for such a property. According to their view, in traumatic tetanus, and in strychnia tetanus, the reflex function of the spinal cord is greatly heightened, so that a slight irritation sets free in the cord an excessive discharge of nervous force, so strong indeed that overstepping the part of the cord functionally connected with the irritated nerve, it may spread, and excite a discharge of force throughout the cord. In other words, they believe that in health a discharge of force is restricted within certain areas of the cord producing co-ordinated action, but in an excited tetanic cord, the resistance limiting the discharge to certain areas is overcome, and the stimulation radiates throughout the reflex portion of the nervous system. This view, therefore, whilst implying a resistance or limiting force, in the central nervous system, possible however to be overcome, implies that this resistance is a constant force incapable of being heightened or depressed by disease or medicines.

Our observations in the paper previously referred to, show that in the tetanus induced by Buxus Sempervirens, and by Gelseminum, the diminution or destruction of the resistance

why do only strong impressions cause irradiation, and why not also weak ones? and then, why does not irradiation extend over the whole sensory centre; whereas it occupies only part of it? We are hereby led to an assumption which we shall render probable also by other reasons; namely, that the excitation has to overcome resistance in the ganglionic cells, and, on account of it, undergoes a loss in its intensity." Not only may impressions radiate in sensory centres, but "it also happens that the pain may cause reflex cramps. Then the stimulus is so great that in spreading out through the neighbouring sensory centres it is not yet reduced to its liminal value, and it then enters motor centres, first of all such as are situated on the same level with the irritated sensory centres and the spinal cord." Speaking of strychnia tetanus, he says, "It is simply due to a depression of this resistance in the nervous centres."

is the sole cause of the tetanus. To make ourselves clear we draw attention to the fact that both box and gelseminum are powerful depressors of the reflex function of the spinal cord, and that in full doses they soon produce complete paralysis of the cord.

In a frog poisoned by either drug we get first great weakness; the animal hops with difficulty, or perhaps can barely crawl, effects due to the action of the poison on the spinal cord, then tetanus supervenes. But the tetanic paroxysms, though very distinct, are in many instances slight. At one period we can get either a normal co-ordinated action or tetanus, according to the degree of stimulation, a weak stimulus producing a co-ordinated reflex act, a stronger stimulus, tetanus. At this time, as the tetanus grows stronger, the normal co-ordinated reflex action is growing weaker; and after a short time, tetanus also grows weaker, and ultimately slowly declines, till at last it is expressed only by slight quivering in all the muscles of the body. Now here we maintain that at the onset of the tetanus there is no increased excitability of the cord, but the very reverse state—paralysis: for the tetanus is preceded by paralysis of the cord. As the tetanus becomes more marked, normal co-ordinated action grows less, shewing that paralysis of the cord is progressing; and at last tetanus itself becomes excessively feeble, shewing that the cord is almost exhausted and paralysed. If then we have no increased excitability, how does it happen that an impression, say to the tip of one toe, after reaching the cord is not restricted to its proper portion of the cord, but diffuses itself throughout it, causing a general, but weak, evolution of nervous force, and consequently a weak, but general, contraction of the muscles, that is to say, tetanus? This can be only explained on the supposition that some change has taken place in the cord, whereby a stimulus is no longer confined to a part of the cord, but can diffuse itself; that some restraining or localizing influence is reduced or destroyed, and to this is given the name "resistance."

Further, we found that in brainless frogs after two or more days, when reflex action had begun to decline, on striking the animal between the shoulders we induced tetanus, and as co-ordinated reflex action grew weaker, the tetanus meanwhile

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became stronger, and was more easily induced; and in some cases, a few hours before the cessation of reflex action we excited strong tetanus lasting half a minute to a minute, the animal becoming rigid from the powerful muscular contractions. Now we submit that in these cases the tetanus could not be due to increased excitability, unless it is maintained that the operation excited inflammation of the meninges of the cord, a supposition highly improbable, for various reasons. We maintain that the tetanus is due to diminution of the resistance in the dying cord, enabling a powerful stimulus, as a blow on the trunk, to spread throughout the cord, and produce tetanus. For further details we must refer the reader to the paper we have mentioned.

We now record some additional observations we have lately made. These we think conclusively prove that tetanus is not always due to increased excitability of the cord. These observations, too, constrain us to admit a resistive power susceptible of modification, the other functions of the cord remaining but little or not at all affected. We pithed[1] and destroyed the brain of three frogs, and then watched for the decline of reflex action. On the third day this was much weaker; in one frog so weak that, on pinching a toe, it only feebly withdrew its legs. We then injected under the skin of the back $\frac{1}{1500}$ grain of strychnia, which in about half an hour induced tetanus. This was very weak in the frog whose reflex action was nearly annulled, and the tetanus in this instance, though distinct, was feebler than the amount of muscular force developed in a normal vigorous reflex act; in other words, the reflex act, though tetanic, was weak.

In the other two frogs, with reflex power much less weak before the injection, we induced strong tetanic convulsions on the slightest irritation, or even shaking the table, the paroxysms lasting a minute or longer. Next day, however, the tetanus was much weaker, and about equal to the tetanus induced by strychnia in the frog with very weak reflex power. The tetanus grew weaker and weaker, but persisted till all reflex action became extinct; and for some time before this, the muscular

[1] Perhaps it is hardly necessary to say that by the term pithed we mean division of the cord opposite the occipito-atlantal membrane.

force displayed after stimulation was far less marked than that occurring in a normal co-ordinated reflex act. We again had weak tetanus excited in a weak and dying cord. These experiments we several times repeated.

Now we venture to maintain that it is impossible to explain this tetanus otherwise than on the supposition of a resistive force, which the strychnia weakened or destroyed. It certainly cannot be explained on the supposition that strychnia simply produces increased excitability of the cord. We are not now denying that strychnia may "excite" or "stimulate" the cord, but admitting this, the tetanus we have just described cannot be due merely to this increased excitability; for were this so, the strychnia should have first improved, then completely restored normal co-ordinated reflex action, and then, on the cord becoming still more "stimulated," tetanus ought to have supervened.

It may be objected that with brainless frogs in a few hours or in two or three days the afferent and efferent nerves become depressed as well as the spinal cord; and hence, though strychnia may restore the lost functional activity to the cord, yet as the impression conveyed thereto is weakened, and the conductivity of the motor nerves is also depressed, the tetanus itself ought to be very weak. We therefore devised the following experiment:—We pithed and pegged a frog, and after tying the femoral vessels of the right leg close to the trunk, we injected into the abdominal cavity a mixture containing one grain of extract of Calabar bean, and $\frac{1}{120}$ grain of strychnia. The Calabar bean we used to depress the cord, and as we wished to induce depression of the cord without effecting any alteration in the afferent or efferent nerves, we tied the vessels of the right leg, thus protecting the tissues below the ligature from the effect of the drug. In twelve minutes slight tetanus set in, the legs on strong mechanical irritation being powerfully shot out once, and once only, after each stimulation. Co-ordinated and tetanic reflex action persisted simultaneously; that is, a weak stimulus excited co-ordinated action, a stronger, the tetanic extension of the legs just described. The co-ordinated reflex action grew weaker and weaker, the tetanus at first remaining undiminished, then it also declined. In this

experiment the action of the Calabar bean at once reduced the cord to the same condition as in a frog which has been pithed two or three days, but of course without depressing either the afferent or efferent nerves of the ligatured leg.

Our argument is otherwise strikingly supported. In brainless frogs (frogs pithed and pegged) reflex action often declines much more quickly in one hind leg than in the other. To a moderate sized frog with very unequal power in the hind legs, one leg being rather vigorously withdrawn on irritating its toes, whilst the other was only partly withdrawn, we injected under the skin of the back $\frac{1}{1600}$ grain of sulphate of strychnia. In half an hour slight tetanus set in, first in the weaker leg, being for some time decidedly stronger in this leg. Now if strychnia tetanus is simply due to "stimulation," in other words to increased excitability of the cord, then the tetanus should certainly have first shown itself in the stronger leg, as it would naturally require less stimulation to induce tetanus in this than in the weaker limb. We noticed also that at a time when the tetanus was so slight that we doubted if it were present, by exercising the limbs and thus weakening co-ordinated action we induced decided tetanus, which rest again weakened, at the same time strengthening co-ordinated action, and strong tetanus could be again induced by a second time weakening the cord by exercising the limb. Now were strychnia tetanus due simply to "stimulation" (increased excitability), it is obvious that the very reverse should have happened.

A similar fact is often witnessed in disease, when paralysed limbs sooner become tetanized by strychnia than other parts of the body, as in the case of hemiplegia from brain disease. Here half the cord is not exercised at all or but slightly, and consequently its nutrition becomes defective, and it wastes. Strychnia will induce tetanus more readily in this depressed half of the cord than in the opposite healthy half.

But it may be said we admit a resistive force which may be overcome, and as the cord dies—as the reflex function diminishes—this resistance will *pari passu* decline; so that with a slight improvement of the reflex function, the evolution of nervous force in one part of the cord will overpower the weakened resistance, and spread throughout the cord. This position

concedes at once that the resistance is alterable in amount, thus admitting a part of our contention. But the explanation in question is altogether inadequate to explain the very different effects of paralysers of the cord. Thus to compare three drugs —Physostigma, Gelseminum, and Box: Physostigma paralyses the cord without producing tetanus; Gelseminum paralyses the cord, and produces weak tetanus; Box paralyses the cord, and excites strong tetanus. How are we to interpret these different effects? Why do Box and Gelseminum tetanize, and not Physostigma? Why should Box tetanize far more than Gelseminum? Before attempting to explain this apparent anomaly, we must interpose two preliminary considerations:—

1. That tetanus is producible only in two ways, either by increasing the excitability of the reflex function, so that the evolution of force may be sufficient to overcome the normal "resistance," and spread throughout the cord; or the "resistance" itself being diminished, an impression conducted to a cord with its reflex function in a normal or even in a depressed state, can overcome the weakened resistance, and affect the whole reflex portion of the cord.

2. It is quite inconceivable that a drug should simultaneously both depress and stimulate (increase excitability of) the same function.

Now, Gelseminum and Box, whilst they both tetanize the cord, depress at the same time the reflex function, and consequently cannot possibly produce tetanus by "stimulating" the cord. Their tetanizing action therefore can be explained solely by their power to diminish "resistance." The difference in the amount of tetanus, produced respectively by Gelseminum and Box, we explain by inferring that Gelseminum induces considerable cord paralysis with weak tetanus, the poison exerting a greater effect on the "resistance" than on the reflex function, and the difference being but slight, we get weak tetanus. Box produces cord depression with much stronger tetanus, showing that the drug exerts an effect far greater on the resistance than on the reflex function; and the resistance being greatly weakened before the reflex function is much

depressed, tetanus excited by Box is far stronger than that from Gelseminum.

Granting therefore that whatever depresses the cord will diminish resistance, we must admit, that some remedies manifest a greater power over resistance than over the reflex function; and when the depression of resistance is greater than the depression of reflex action, we get tetanus. The relative effect on the reflex and the resistive functions well explain the various degrees of paralysis associated with tetanus, and the strength or weakness of the tetanus itself.

We would suggest that conceivably we may have four combinations in tetanus.

1. Tetanus with increased excitability and normal resistance of the cord.

2. Tetanus with increased excitability, and diminished or destroyed resistance of the cord.

3. Tetanus from mere diminution of resistance.

4. Tetanus with depression of the reflex function and diminished resistance.

We have adduced in this paper sufficient evidence of the fourth form of tetanus, and have elsewhere expressed a doubt if the first and second kinds of tetanus ever occur.

Surely, it will be said, the strong tetanus of strychnia must be due to increased excitability of the cord, as well as diminution of resistance; for in a paroxysm, induced by even a slight irritation, the amount of muscular force, and *ergo* of the nervous force developed in the cord, is far greater than occurs in a normal co-ordinated reflex act, and this excessive evolution of force proves the increased excitability of the cord. But we think that strychnia tetanus is best explained by simply temporary diminution or abolition of resistance. For we have shown in the pamphlet already referred to, that loss of resistance, even with depression of the reflex function, will produce strong tetanus. This is the case with Box. This drug, as we have seen, produces first partial cord paralysis; then strong tetanus ensues, whilst the co-ordinated reflex contractions, which can be induced by weak stimulation, are at the same time

growing progressively weaker; that is to say, we get strong tetanus with progressive cord paralysis.

In order to explain these strong paroxysms when the evolution of nerve force is far greater than that occurring in a normal co-ordinated act, it is obvious we must assume that the resistance not only restricts impressions to certain areas of the cord, but that it also limits the amount of force evolved; in fact, by paralysing "resistance" we not only allow a stimulus to spread throughout the reflex portion of the cord, but also to set free an increased amount of nervous force from every portion of the cord and motor parts of the brain. In other words, the function or condition to which the name "resistance" is given not only localises but restrains reflex action in the spinal cord. If then, in the case of Box, we get strong tetanus with slight depression of the cord, we think it possible that the still stronger tetanus of strychnia may be due simply to depression of this resistive function without any increased excitability. Hence, as in the case of Box, but in even greater degree, a slight stimulation not only spreads throughout the cord, but sets free an excessive amount of nervous force.

It will probably be objected that if diminution of resistance permits also the evolution of an excessive amount of force—that resistance in fact not only localises but restrains or controls the amount of reflex action—then, as resistance becomes weakened, the co-ordinated reflex acts should become stronger; as in that stage of Box and Gelseminum poisoning, when, according to the strength of the irritation, we obtain either a co-ordinated or a tetanic reflex act, the co-ordinated act should become stronger. This is not true of Box and Gelseminum poisoning, probably because, as the tetanus sets in and grows more severe, the paralysis of the cord progresses quickly, so that any increase in normal co-ordinated action due to diminution of resistance would escape detection; though we must grant that this paralysis should likewise weaken the tetanic reflex act. In strychnia poisoning, where there certainly is no weakening of reflex action, the co-ordinated reflex acts on the onset of tetanus do become stronger, as the following observation repeated several times establishes. We pithed and pegged a frog, and when reflex action had considerably declined, but the

limbs were still withdrawn under the stimulus of pinching or electricity, we suspended the brainless animal, by passing a pin through the lips, and pinning it to a retort holder, so that it hung with its legs suspended, and then injected $\frac{1}{1500}$ grain under the skin of the back, and watched for the onset of tetanus. With this small dose tetanus came on slowly, remaining for a long time comparatively weak, so that a slight irritation induced a co-ordinated reflex act; a stronger one, tetanus. In this stage we found that co-ordinated reflex action was much more easily and powerfully induced than before tetanus set in. Thus, before the injection of the strychnia only the irritated leg was withdrawn, and once only, and then again relaxed; but after the setting in of tetanus the leg, in a co-ordinated act, was first withdrawn on slighter irritation; next, as tetanus increased, both legs were withdrawn; and later, both were withdrawn and extended several times, with even a very slight stimulus, as, for instance, the very slightest touch. This effect of strychnia was still better exemplified by the following experiment. A frog, pithed and pegged seventy-one hours beforehand, we suspended by a pin passed through the lips and fixed to a stand, on each side the right ankle we placed the thin wires of the electrodes, tying them to the ankle by waxed thread, then by means of Du Bois Reymond's induction coil we ascertained the weakest current capable of exciting a reflex act. Then we injected $\frac{1}{1500}$ gr. of strychnia under the skin of the back, the instrument standing at 10·5, and as tetanus gradually set in a weaker current was sufficient to produce a co-ordinated reflex act. Thirty-four minutes after the injection, reflex action was induced with the coil standing at 11; in an hour, at 12; in an hour and twenty minutes, at 13; in an hour and a half, at 14; in an hour and forty minutes, at 16. Surely this, an objector might say, is increased excitability of the cord. Of course strychnia so affects the cord that a slight stimulus evokes a very great discharge of nervous force; but the question we raise is this:—Does this increased evolution of nervous force depend on some alteration in the composition of the cord elements, so that chemical changes and consequently the production of force are more easily induced; or is this increase

of force due to weakening or destruction of some controlling power which has been termed "resistance"?

In support of the theory of resistance, we must again refer to the effect of Box on the cord. This drug first produces cord paralysis, and whilst this quickly advances, strong tetanus occurs, which, as we have said, cannot be due to increased excitability, but must, we think, depend on loss of "resistance" of the cord; and we suggest that it is at least feasible that even the strong tetanus of strychnia may depend simply on loss of resistance, though as the reflex function is in no degree weakened, this tetanus is more powerful than that of Box.

We here adduce some observations confirmatory of this view.

In a brainless frog, after three or four days, reflex action so far declines that it cannot be excited in the smallest degree by stimulation of the extremities; but a sharpish blow over the spine produces slight and general muscular contraction. On repeating the blows, the muscular contraction grows stronger and stronger, at last becoming decidedly tetanic; and now if the blows are still continued, the muscular movements become abolished. These effects we explain in the following way:—The blow on the back diminishes the "resistance" at first very slightly, and though all the muscles are affected they contract but slightly; a repetition of the blows, of the same strength, reduces the resistance more and more, and with each blow a greater amount of nerve force is evoked; that is, the amount of stimulation remaining the same we produce a far greater amount of muscular contraction. Repeating the blows still further, we depress the cord, and at last abolish all reflex action. The increased evolution of nervous force in the cord can be explained, we think, only by the fact of diminished resistance. The augmented evolution of nervous force cannot be due to excitement of the cord, since in this experiment there is nothing to suggest or to explain the increased excitability, and, as we have said, we took care that the blows should be as nearly as possible of the same strength. If this explanation be accepted, then it shows that through diminution of resistance a greater force is evolved with the repetition of a stimulus always of the same strength.

Now if we give a dose of strychnia to a frog in the condition just described, in a short time, when absorption has taken place, we bring the cord of that animal to the condition of the frog which has undergone a repetition of blows on the back; that is to say, one blow will produce a decided, though weak, tetanic contraction. Here the strychnia acts like the repeated blows, weakening resistance, so that a stimulus will evoke a greater amount of nerve force than would have occurred before the resistance was depressed.

ON THE EXTENT TO WHICH ABSORPTION CAN TAKE PLACE THROUGH THE SKIN OF THE FROG. By WM. STIRLING, D.Sc., M.D. *Demonstrator of Practical Physiology in the University of Edinburgh.*

(From the Physiological Laboratory of the University of Edinburgh.)

IN some experiments which I was making upon frogs I chanced to leave some of these animals on a plate containing a small quantity of water, the whole being covered by an ordinary bell-jar, with a piece of moist blotting paper inside it, in order to keep the atmosphere surrounding the frogs quite moist. Next morning I found that the abdomen was very much distended, a male frog presenting quite the appearance of a female one distended with ova. This was due to the enormous distension of the bladder with fluid which had evidently been absorbed through the skin.

Determining to test to what extent absorption of water may take place through the skin of frogs in a given time, I first destroyed the brain and spinal cord as far down as the second cervical vertebra. The spinal canal was plugged to prevent hæmorrhage, and the frogs being then carefully weighed were placed in a plate covered with a layer of water about one-eighth part of an inch deep, the atmosphere being kept moist by placing a bell-jar over the plate. The frogs were allowed to remain under these conditions for twenty-four hours and then weighed again, the difference in weight of course representing the amount of water absorbed. The following table represents the results I obtained by this method in the first four frogs.

Nos. 5, 6, and 7, instead of being laid flat upon a plate containing water, were suspended in a jar of water. The water reached up nearly to the axilla in all three cases.

	Original Weight in Grammes.	Weight in Grammes after being 24 hours in water.	Difference in Grammes.	Per cent. of Body-Weight.
Frog 1	22.6	27.01	4.41	19.5 per cent.
" 2	22.25	27.9	5.65	25.4 " "
" 3	27.45	30.5	3.05	11.1 " "
" 4	28.2	32.04	3.84	13.6 " "
" 5	26.2	30.25	4.05	15.4 " "
" 6	21.1	25.2	4.1	19.4 " "
" 7	23.95	29.6	5.65	23.6 " "

These results show that the amount of fluid absorbed varies in each individual case, and that a very active absorption of water takes place through the skin of frogs so treated, amounting in one case to over 25 per cent. of the original weight of the animal. This is a very great increase, and may be accounted for by the extremely rich net-work of vessels ramifying in the frog's skin, and the ready osmosis which takes place through the skin of a frog, even when stripped off like a glove from the limbs. That various substances can pass through the frog's skin has been recently shown by A. v. Wolkenstein[1]. In my experiments the water absorbed must have passed into the circulation, and was then excreted by the kidneys. The facilities for absorption were no doubt increased in these cases by the destruction of the vaso-motor centre in the medulla, which would be followed by dilatation of the vessels of the skin, thus giving a larger area through which absorption could take place. The whole of the water absorbed, however, did not pass into the bladder, for on measuring the amount of fluid expressed from the bladder, it was always found to be considerably less than what was actually absorbed.

[1] *Centralblatt für die Med. Wissensch.* 1875, No. 26.

This is shown in the following table:

	Actual increase of Weight in Grammes.	Fluid expressed from Bladder.
Frog A.	4	3.5 cc.
„ B.	4.1	3.55 „
„ C.	6.15	4.66 „

This extra fluid must therefore have passed into the circulation, and so diluted the blood. That it had much effect on the blood-tension is not at all likely, for we know that a very considerable volume of blood may be added to the circulation without any permanent increase of the blood-pressure, as was shown by Worm Müller[1]. No increase in the amount of fluid was observable in the lymph-sacs.

With regard to the amount of fluid absorbed in a given time, I obtained the following results:

	Increase of Weight in $6\frac{1}{2}$ hrs.	Increase of Weight in 24 hrs.	Increase of Weight in 48 hrs.
Frog a.	1.3 grammes	4.0 grammes	4.0 grammes
„ b.	2.9 „	4.1 „	7.0 „
„ c.	2.65 „	5.65 „	6.15 „

This table clearly shows that the amount of fluid absorbed is relatively very much greater during the first six hours of immersion than during the next 18. The increase also in the second 24 hours in one case was nothing, and in another only ·5 gramme. This may be explained partly by the increase of the amount of fluid within the blood-vessels, thus diluting the blood and, it may be at the same time, increasing the blood-tension. Another factor tending to the same result is the tension within the bladder, owing to its having become so distended, preventing the entrance of more fluid into it, thus leading to diminution in the amount of urine secreted, or it

[1] Ludwig's *Arbeiten*, 1873.

may be suppressing the reaction entirely. The result of this would be, that little or no fluid would be withdrawn from the circulation by the kidneys. Another factor may be, that the bladder, by being so greatly distended, might press upon the heart, and so interfere with its movements. It is interesting to note, that if the bladders of these frogs were again emptied, they became filled, *i. e.* absorption went on, just as before.

In order to test whether the destruction of the vaso-motor centre facilitates the absorption, I removed only the brain in some cases. There is in these cases, however, great difficulty in preventing the frogs from emptying their bladders; but I found that they did not absorb so much fluid as those in which the upper part of the cord was divided.

Remembering how rapidly sulphindigotate of soda is excreted by the kidneys when introduced into the circulation, I placed several frogs in a watery solution of this blue colouring matter, but the result, as far as the absorption of the colouring matter was concerned, was negative, none of it passing through the skin, although the water passed through, and was excreted by the kidneys, just as if ordinary water had been employed.

A similar negative result was obtained with a watery solution of Berlin blue.

On suspending a frog, in which the vaso-motor centre and the brain were destroyed, in a weak solution of sulphate of strychnine, within two or three hours the frog exhibited the characteristic tetanic spasms. Further, after immersion of frogs for 24 hrs. or so in a solution of ferrocyanide of potassium, this substance could easily be detected by the ferric chloride test, giving a blue colour with the urine expressed from the bladder.

On opening the abdomen of such animals with their bladders distended, it was very prettily shown that the bladder, in the case of the frog, is bilobate, each lobe extending laterally and upwards into the abdominal cavity. A firm bridge of tissue, containing a blood-vessel, runs from above downwards in the anterior wall of the bladder, binding it down, and giving it its bilobate appearance.

ON CERTAIN MOLAR MOVEMENTS OF THE HUMAN BODY PRODUCED BY THE CIRCULATION OF THE BLOOD. By J. W. GORDON.

A PERSON standing erect in a perfectly easy posture on the bed of an ordinary spring weighing-machine, and maintaining, as far as possible, perfect stillness, will be found, if the instrument is delicately adjusted, to impart a rhythmic movement to the index, synchronous with the pulse and according to the following rule:—At each occurrence of systole in the heart, the needle will be vigorously deflected toward the zero point of the dial, and in the intervals of systolic action will return by a slower movement to the starting point; this point nearly coinciding with the point at which the needle would rest if the subject were laid horizontally on the bed of the instrument. The return of the needle is effected by a series of secondary vibrations which appear to bear an appreciable but imperfect analogy to corresponding features in the sphygmograph.

This phenomenon may very easily be verified, but in repeating the experiment it should be borne in mind that the following are desiderata:—That the skeleton of the subject be brought as nearly as possible into contact with the instrument and that the hip- and knee-joints be so disposed as to secure the *maximum possibile* of rigidity in a perpendicular direction. It does not appear that this phenomenon has heretofore been anticipated by any process of theorising, or turned to any useful account. It may therefore be permitted me to point out what may prove to be its phenomenal cause and practical consequences.

As to its cause—When the heart is contracting it propels blood in all directions; but the greatest column is propelled downward, along the aorta, almost in the direction of the axis of the body. If, therefore, we disregard all blood that is propelled upward, and make a compensating abatement from that which is propelled downward, there will remain a certain mass of blood which at each contraction of the heart is forced

vigorously downward, and which therefore must give rise to a recoil in the opposite (*i.e.* upward) direction. Indeed, the case is precisely analogous to that of a ball propelled from a gun, and in both cases the vis inertiæ of the body propelled is the principal cause of the reaction. It is worthy of remark that the analogy is not vitiated by the fact that in the one case the body propelled does and in the other case does not get free of the system to which it originally belongs. For, take the case of the gun: Here the reaction is set up while the ball is still in the barrel; as soon as the ball passes the muzzle, and the confined gas behind it is set free, it can communicate no more motion to the gun. Suppose then a target of sufficient strength attached to the gun and held at a short distance in front of the muzzle. In this case the ball will never get free of the system to which it originally belongs, but its opportunity of generating recoil will not be impaired by this arrangement, although the recoil will be almost immediately checked. This is precisely what occurs in the human body. The projected mass of blood is checked in its course, not indeed by any rigid diaphragm, but by the elastic walls of the arteries through which it flows. But *so long as it is actually in motion the analogy to a gun is complete.*

This raises another point. Whether there is any actual reflux of blood in the principal arteries, or whether the flow is continuous, but variable, is not assumed in the above proposition, for the motion there referred to is relative. For example; assuming that the inward flow of blood in the venous system compensates the outward flow in the arterial, it will be evident that the mean, *i.e.* actual, velocity of the venous flow must lie between the extreme velocities of the arterial flow[1]. When, therefore, the velocity of the arterial blood is such as only to compensate (or produce momentum equal to that produced by) the venous flow, this blood would be said to have no relative motion; when it falls below this speed there is a relative reflux, and a recoil is produced in the opposite direction. If therefore the vascular system be con-

[1] More accurately—the momentum generated in the venous system must lie between the momentum generated by the extreme velocities of the arterial flow; for if the area of the venous system : area of arterial system $=9:4$, the arterial flow at its slowest might conceivably be quicker than the venous.

nected with a weighing-machine by means of tolerably rigid supports, we ought to have an observable effect produced on the weight of the body, whenever the posture is such that the blood which flows through the descending aorta has a virtual velocity in the direction of gravitation.

With these facts in view probably my readers will concur in referring the phenomenon to the cause suggested here. It remains to discuss the best method of deriving a sphygmograph from the motion thus caused. The most obvious method of effecting this is to allow the index of a weighing-machine, such as is described above, to trace out a figure in the ordinary sphygmographic manner. By such a process Fig. 1 has been produced; of which it may be remarked that the second deflection behaves in such a manner as to leave but little doubt of its being a representation of the dicrotic wave. With less certainty the third deflection may be referred to the tricrotic wave.

Fig. 1.

Fig. 2.

In Fig. 1 the downstroke which is immediately succeeded by a long upstroke is synchronous with the systole: the next downstroke is the second deflection referred to in the text. The upstrokes are to be regarded merely as indicating the instrumental tendency to restore equilibrium.

In Fig. 2 the letters bear the same significance as in Dr Galabin's figures. Vide infra.

It has, however, been found possible to substitute for this process one much more satisfactory in every respect. It will be obvious that if the subject be placed in a horizontal position, the internal movements which in the perpendicular position caused the weight to vary, will now tend to produce horizontal motion; and if the body be free to move will actually produce a movement, the observation and registration of which will be a matter of delicate measurement only. By employing the horizontal position several important advantages are gained, *e.g.* much greater proximity of the skeleton to the supporting framework

can be secured; and the resulting figure conforms to the ordinary sphygmographic type, whereby the task of analysing it is greatly simplified. Accordingly Fig. 2 was produced in the following manner. A frame constructed in the lightest possible form, of sufficient size to allow the body of the subject to be disposed at full length upon it, was swung by four ropes from a trestle of appropriate size, and substantial structure. This frame was fitted with sliding supports, upon which the body was sustained by contact at those parts where the soft tissues are thinnest, *e.g.* the spine towards its extremities, the sacrum, ilia, and scapulæ. The body thus supported hammock-wise has a movement corresponding to that observable by means of a weighing-machine, and, with a sphygmograph adapted to the circumstances, yielding figures like the one already referred to.

It will be observed that the curve so obtained is remarkably conformable to the type which has been ascertained, by experiments made under special circumstances, to be characteristic of the aortic flow. If Fig. 2 be compared with the aortic tracings which illustrate Dr Galabin's paper on "Transformations of the Pulse-wave," *Journal of Anat. and Phys.*, Vol. x. p. 297 (see especially figs. 42 and 46, Pl. XIV.) the correctness of this statement will be obvious. I would especially call attention to the small rise Z preceding the main up-stroke.

It would seem therefore that the production of a sphygmograph from the aortic flow in a human subject under perfectly normal conditions is a matter of no difficulty. Moreover, the process which, though indirect, yields results of astonishing delicacy, is capable of being most extensively and instructively varied.

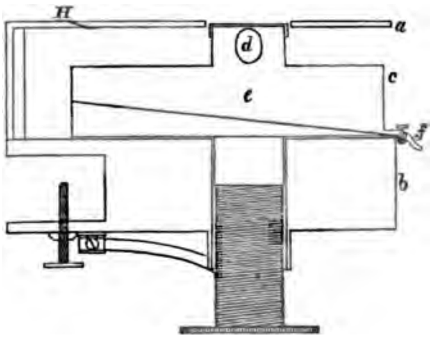
ON A NEW FREEZING MICROTOME FOR THE PREPARATION OF SECTIONS OF THE BRAIN AND SPINAL CORD.—By BEVAN LEWIS, F.R.M.S., *of the West Riding Asylum, Wakefield.*

THE older method of hardening tissues by chromic acid and its salts, preparatory to section-cutting, will, I think, be generally acknowledged as inferior in many respects to the more elegant method of freezing, for, besides the dehydration which is produced, we dare not presume, with our present knowledge, to affirm that objectionable chemical changes may not result which might unfavourably affect the appearance natural to the tissue elements in their physiological or pathological state. One point is certain, and that is, that the process *does materially interfere* with the staining and differentiation obtainable by perfectly fresh preparations mounted in glycerine and indifferent media. All these objections apply with tenfold force to the delicate structures of the nervous system, where the dimension of cells, the tracing of minute fibrils, connecting branches, and the neuroglia basis are all more or less modified from the conditions natural to them during life. That this assertion is not made hastily, any one may satisfy himself of, by contrasting the appearances of freshly stained brain made by a process which I have adopted and described in the *Monthly Microscopical Journal* for September, 1876, with those obtained by chromic-acid hardening. The fresh process alluded to, although of real value for the exhibition of minute details in the brain cortex, has one decided disadvantage. I refer to the alteration of the natural relationships of histological elements. This difficulty I endeavoured to overcome by the application of the freezing method, in spite of constant statements made to me to the effect that freezing was inapplicable for sections of the brain cortex. As rapid freezing was desirable, I was compelled to dispense with the use of Prof. Rutherford's elegant microtome, and contrive some apparatus which, by the use of the ether spray, should meet the ends in view. For sections of the brain and spinal cord I find the microtome thus devised invaluable, no imbedding being required and the tissue being frozen sufficiently hard for the finest possible sections to be cut from it in from *twenty* to *thirty seconds.* I have obtained also by its use most satisfactory sections of the solid viscera of the abdomen, but chiefly employ it for sections of the nervous system.

The instrument consists of three portions: (1) an ordinary Stirling's microtome; (2) a section-plate; (3) a freezing and condensing chamber. The simplicity of the arrangement will, I trust, recommend its use amongst my fellow-workers in the department of cerebral histology.

Reference to the accompanying woodcut will place the reader in possession of the plan upon which this instrument has been constructed. The section-plate (*a*) is riveted by a brass arm to the microtome (*b*). The freezing compartment (*c*) consists of a cylinder

(*d*) and a condensing chamber (*e*), the latter being formed of brass with a sloping floor leading to the exit-tube, which is provided with a



stop-cock (*f*). The cylinder is capped with tin-foil stretched across it and has an orifice (*d*) through which the nozzle of the spray apparatus is introduced. In using this instrument it is only necessary to bring down the cap of the cylinder from one-fourth to three-eighths of an inch below the level surface of the section-plate, and to place in it a section of brain of about the same thickness. The spray instrument is inserted at the orifice, and by the ordinary double elastic balls a free play of ether beneath the cap freezes the tissue in from twenty to thirty seconds or less. On withdrawing the spray instrument, the slight play of ether, still continuing from the remaining tension of the elastic ball, is utilised by being carried rapidly along the surfaces of the section-blade, and then the finest possible sections may be cut with great ease. The consistence of nervous structures, when thus frozen, is really exquisite for section-cutting, and the tissue remains rigidly adherent to the capped top of the cylinder.

Perfect steadiness of the freezing chamber is ensured by soldering it to the microtome plug, and it can be readily removed from its position by throwing back the section-plate, a movement allowed for by the hinge-joint (*H*). The advantages accruing from the use of this simple instrument are sufficiently obvious with regard to sections of the brain and spinal cord. The tedious process of chrome-hardening, occupying the period of three to four weeks, or longer, is reduced to one of extreme simplicity, in which a few seconds give us the same results; the sections thus produced being in every way as delicate and thin, and free from the injurious effects of chemical reagent, no shrinking of tissue being recognised and the film remaining in the most perfectly natural condition as regards relationship and size of its individual elements. Nor is this the only result obtained, for, sections thus prepared, immediately demonstrate the antagonistic action of the hardening reagents in the succeeding stages of staining and differentiation. Sections by the freezing process retain their susceptibility for staining to a degree never met with in the latter, the results being in every respect equal to those obtained by the fresh method before alluded to.

I would, therefore, claim for this method all the advantages of the older process of hardening, together with those of the fresh teasing method, whilst the disadvantages of the former are entirely averted; and on these grounds I see no reason why it should not take precedence in the preparation of the nervous structures for physiological and pathological purposes.

[After writing the above article I was referred, through the courtesy of Prof. Turner, to the *Journal of Anatomy* for April, 1876, where I find that the principle of freezing by ether had already been adopted by Mr Hughes. In his Microtome, however, the spray is not so directly brought to bear upon the tissue, which consequently requires from five to eight times as long a period to freeze, with, of course, a corresponding increase in the loss of ether: this is of material import when absolute anæsthetic ether is employed.]

NOTE ON A CONNECTING TWIG BETWEEN THE ANTERIOR DIVISIONS OF THE FIRST AND SECOND DORSAL NERVES.—By D. J. CUNNINGHAM, M.D., *Senior Demonstrator of Anatomy in the University of Edinburgh.*

IN the course of my dissections of the spinal nervous system of the Porpoise and Dolphin[1], I was interested to find in the latter a well-marked branch given to the brachial plexus by the anterior division of the second dorsal nerve. In a conversation with Professor Allen Thomson, of Glasgow, during the last meeting of the British Association, I instanced this as being one of the few points in which the brachial plexus in these animals differed from the brachial plexus in man. I was surprised when Professor Allen Thomson told me that he had on one or two occasions seen such a nerve in the human subject, and that he believed it to be not at all an unusual occurrence. In the last edition of Quain's *Anatomy*, however, there is no reference to it, nor indeed is it mentioned in any of our text-books. It is curious also to find it altogether unnoticed in Henle, Hirschfeld and Leveillé, and in "The Anomalies of the Nerves," by Krause.

Judging this, therefore, to be a matter of some little importance, I determined to make a number of dissections of the second dorsal nerve, in order that the question might be cleared up. By these I have made out that the connecting link between the second and first dorsal nerves is present, in some form or other, so frequently, that it almost deserves to be considered as a normal arrangement. The following is the result of these dissections:—

Frequency of Occurrence.—In all I have made 37 dissections. In ten of these I failed to find the branch in question, but five of

[1] Vide *Journal of Anatomy and Physiology*, Vol. XI. Jan. 1877.

these cases must be regarded as being doubtful, either from the fact that the part had been previously interfered with by the dissector of the thorax, or from the dissection having been rendered difficult by pleuritic adhesions and thickening.

Size.—In the 27 cases in which I found it, it varied greatly in size. Sometimes it was very large; at other times extremely fine, and seen only with difficulty. In one case, that of a child, apparently about four years old, it was quite as large as the ulnar nerve in the same subject. This is to be regarded, however, as very unusual, because, as a rule, it is very small, and certainly not larger than the nerve of Wrisberg. Sometimes it is double; and on one occasion there were three present on the same side, all of course being minute.

Connections.—It springs from the anterior primary division of the second dorsal nerve, close to its origin; it passes up over the neck of the second rib in close relation to the branch from the superior intercostal artery, which descends to the second intercostal space, and usually ends by joining both the brachial and the intercostal divisions of the first dorsal nerve. It may, however, end entirely in the one or in the other; when it is double, one goes to each of the divisions of the first dorsal nerve; and in the solitary case, where there were three twigs, two went to the brachial division and one to the intercostal division. In passing up in front of the neck of the second rib it is frequently joined by sympathetic filaments.

I regret that I have not sufficient data to prove whether or not this little nerve from the second dorsal to the brachial plexus is influenced in its size by that of the intercosto-humeral branch of the same nerve. It is my strong impression, however, that it is, because in one case where I had an opportunity of examining both, I found that the connecting nerve from the second dorsal to the plexus was very large, whilst its intercosto-humeral branch was extremely small; further, the lesser internal cutaneous in the same subject was somewhat larger than usual.

REPORT ON PHYSIOLOGY. By WILLIAM STIRLING, D.Sc., M.D., C.M., *Demonstrator of Practical Physiology in the University of Edinburgh*[1].

NERVOUS SYSTEM.

Brain.

ON THE FUNCTIONS OF THE BRAIN IN THE NEWLY-BORN.—O. Soltmann (*Jahrb. für Kinderheilk.* Band IX. and *Centralblatt*, No. 23, 1876).—The chief differences in the structure of the brain of the adult and the newly-born exist specially in the cerebrum, as the seat of the will and intelligence. The author experimented, after Hitzig's method, on newly-born rabbits and dogs, to ascertain whether the movements which are discharged by the impulse of the will from the gray matter are also present in the newly-born. It was noticed that in removing the dura pain was produced, but no convulsions. It was shown that on the tenth day of extra-uterine life the "centre" for the anterior extremities was formed (*all* other centres were absent), and at this time occupied a greater area than at a later period. The same is true of the area for the posterior extremities, which appears about the thirteenth day. These provinces gradually become limited, and on the sixteenth day they are well-defined (*e.g.* the centre for the anterior and posterior extremities and facialis). No doubt, individual peculiarities and those of race affect the development and localisation of the individual centres. Coinciding with the above, *destruction* of the cortical area within the first ten days produced no symptoms of paralysis or ataxia. Even when the animals survived, no observable disturbances occurred later—even in one dog, where the cortex was destroyed in both sides. At eight weeks this animal was small and plump, and those animals operated on, on only one side, were in a similar condition.

In order to test whether the deeper parts of the brain of the newly-born are excitable or not, isolated needles were introduced and the corpora striata stimulated. By stimulating them it was impossible to produce contractions: but from the fibres of the capsula interna contractions of the opposite anterior extremities were produced. The point to be irritated varied with the individual and with age. It was most certain on stimulating the fibres passing between the corpus striatum and the optic thalamus, even at the time *when no effect could be obtained from the cortex.*

The most probable cause of the absence of effect on stimulating the brain of the newly-born, is probably due to the fact that at so early a period the fibres are not all covered by a white substance of Schwann, so that the channels are not well isolated. How

[1] Authors are invited to send copies of their papers to Dr Stirling, Physiological Laboratory, University of Edinburgh.

imperfect the cerebral functions are may be shown by the following experiment:—Both hemispheres, with corpora striata, of a newly-born dog were extirpated, so that it retained the optic thalami and corpora quadrigemina, and all the movements previously exhibited by the animal took place as before. As a proof that after extirpation of one hemisphere the other may act for the removed one, the author gives the following experiment:—From a dog four days old the whole pre-frontal lobe and part of the post-frontal on the left side were removed. When after three months the *right* centre for the anterior extremity was exposed and stimulated, not only the *left* but also the right forefoot responded.

ON THE ELECTRICAL EXCITABILITY OF THE CEREBRUM OF THE FROG.—O. Langendorff (*Centralblatt*, No. 53, 1876) finds, 1. That stimulation of certain parts of the hemispheres with a weak constant or interrupted current can produce movements of the trunk-muscles in the frog. 2. On simultaneous stimulation of both hemispheres movements occur in all four extremities and some of the muscles of the trunk. On unilateral stimulation movements occur in the trunk, and in the extremity of the opposite side. 3. The "irritable zone" lies in the parietal area. Stimulation of the other parts is without results if weak currents are used. 4. The movements disappear after complete severance of the brain from parts lying more posteriorly. 5. Narcosis from ether abolishes the electrical excitability of the cerebrum, whilst it is not affected by complete vascular depletion. [The results therefore correspond exactly to what has been found in other animals.]

ELECTRICAL STIMULATION OF THE BRAIN.—C. Fürstner (*Arch. f. Psych.* VI. 719) has repeated the Hitzig-Ferrier experiments on rabbits and dogs, and obtained similar results in the muscles, though the 'centres' stimulated differ somewhat from those indicated by Ferrier. After movements were often observed, especially in the area supplied by the facial nerve. Sometimes in dogs circumscribed muscular movements could be obtained by stimulating those parts lying between centres.

"On the Physiology and Pathology of the Cerebral Cortex." A. Eulenburg, *Berlin. Klin. Wochenschr.* No. 42 and 43, 1876.——"On the Functions of the Corpora Quadrigemina." Kohts, *Virch. Arch.* LXVII. p. 425. A clinical case.——"On the influence of the Form of the Skull in the Direction of the Convolutions of the Cerebrum." Ludwig Meyer (*Centralblatt*, No. 43, 1876).

ON THE FUNCTIONS OF THE BRAIN, by Dr D. Ferrier. Smith, Elder & Co., 1877.

Spinal Cord.

"On a difference in the Reflex Functions of the Medulla Oblongata and the Spinal Cord in the Rabbit." Owsjannikow, *Ludwig's Arbeiten*, 1875, 457.——"On Certain Peculiarities of Movements produced by Mechanical Stimulation of the Cranial Dura

Mater." Bochefontaine, *Comptes rendus*, LXXXIII. No. 6, and *Centralblatt*, No. 47, 1876.

MECHANIK DER NERVEN UND NERVEN-CENTREN. Von W. Wundt, Zweite Abtheilung, Stuttgart, 1876. We propose in our next Report to refer fully to this important contribution to our knowledge of Reflex Action.

INVESTIGATIONS ON REFLEX ACTION. J. Rosenthal (*Sitzungsb. d. phys. med. Ges. zu Erlangen*, 10th May, 1875) has continued his researches on this subject (this *Journal*, VIII. 182), and finds that in the normal condition after every sensory stimulation of the lower extremities of a frog there is flexion; after poisoning with strychnine only extensor movements take place. The difference between the "flexor-reflex" and the "extensor-reflex" consists in this, that in poisoning by strychnine the *extension* of the reflex to channels which usually offer great resistance, is facilitated. Poisoning with strychnine facilitates the occurrence of reflex movements. Still this increase of the reflex excitability is quite inconsiderable. The results already (*loc. cit.*) given for the "reflex time," and "time of transverse conduction" are valid, as well for a flexor as for an extensor-reflex. The absolute value of these times is diminished by strychnine. The diminution is more considerable for the time of transverse conduction than for that of the reflex time. The rapidity in the transmission of the excitement in motor nerves is independent of the strength of the stimulus. A stimulus of just sufficient strength gives exactly the same values as over-maximal stimuli. Strychnine poisoning has no effect on the rapidity of propagation of excitement in motor nerves. Cooling of the motor nerves diminishes the excitability very considerably. The reflex time, and the time of transverse conduction, are thereby considerably lengthened, the latter to a greater extent than the former. Although every part of the spinal cord under certain circumstances is able to convey a reflex excitement, still the transference, and especially the transverse conduction, does not take place equally easily in all parts of the cord, and certainly not always at the place where the nerves may enter. The transference of reflex excitement and the transverse conduction take place most easily in the medulla oblongata. If the connection of the peripheral nerves with the medulla is interrupted, stimuli which were previously effective become ineffective, whilst over-maximal stimuli are still active. Weak stimuli always give only a unilateral reflex, strong stimuli a bilateral reflex. The transverse conduction in the cord therefore takes place less easily than the transference of the excitement from the sensory to the motor nerves on the same side of the end. Weak stimuli, of themselves ineffective, may discharge a reflex by being superimposed one on the other. There is therefore a summation of sensory irritations in the spinal cord. [As was shown by the Reporter, *Journal of Anat. and Phys.* x. 304.]

OBSERVATIONS ON REFLEX INHIBITION.—H. Nothnagel (*Arch. für Psych.* Bd. VI.) observed that in several patients suffering from

disease of the spinal cord, and who showed the knee-foot-phenomena (patellar tendon reflex), he could by pressure on the crural or ischiatic nerve of the same or of the other side, cause this phenomenon to disappear on both sides. That in this case it is not due to pressure on the nerve interrupting a convulsive irritation proceeding centrifugally from the cord, is concluded by the author from the circumstance that pressure on the cruralis also inhibits the movements in the area supplied by the ischiatic, and pressure on the nerve-trunk of one limb arrests the movements in the other. There is here rather a centripetal impression, for the pressure affects all the sensory fibres of the nerve-trunk. Stimulation of the expansions of the nerves in the skin (electric stimulation, powerful compression of the limbs) was without effect. In those cases where impressions proceed from a pathologically altered cord, an abnormally strong stimulus must be applied to the trunk of the nerve in order to produce a reflex inhibition. Further, as the galvanic excitability of the nerve-trunks was not increased, nevertheless as pressure exercised on them not only inhibited movements, but also discharged others, the author assumes that there was an increased *mechanical* excitability of the nerve trunks.

General Physiology of Nerves.

"On transverse conduction of currents through Nerves." A. Fick, *Arbeit. aus d. Würzb. Hochschule*, p. 270.——"On partial stimulation of Nerves." H. Munk, *Reichert und du Bois'. Arch.* 1875, 41.——"The transverse conduction through Nerves during stimulation." L. Hermann, *Pflüger's Arch.* XII. 151, and *Centralblatt*, No. 39.——"On unipolar excitation of Nerves." A. Chauveau, *Comptes rendus*, LXXX. 779 and LXXXVI. 1038, and *Centralblatt*, No. 37.——"On the rapidity of the Nervous Current in Sensory Nerves." Bloch, *Arch. de Physiolog.* 1875, and *Centralblatt*, No. 38.

ON THE CONDITIONS FOR THE PERSISTENCE OF SENSIBILITY IN THE PERIPHERAL END OF DIVIDED NERVES.—Arloing and Tripier (*Arch. de Phys.* 1876, 11) arrived at the following results:—1. The facial nerve and spinal nerves of solipeds and rodents, like the carnivora, possess recurrent sensibility. 2. In order to detect it, the parts situate most peripherally must be investigated. 3. The peripheral end of the trigeminus is sensitive. This is difficult to prove, but still it exists. 4. In all cases the peripheral nerve-ends owe their sensibility to nerve-fibres whose connections with the trophic and perceptive centres are not interrupted. 5. If these nerve-tubes are divided, the peripheral end is also insensitive. 6. For the facial nerves these fibres originate from the trigeminus; for the purely sensory nerves (trigeminus) from the neighbouring branches and from the nerves of the other side; for mixed nerves from neighbouring nerves and their own homologues. 7. The recurrent fibres ascend in the nerves to which they are distributed for a shorter or longer distance (centrally); their number diminishes from the periphery to centre. 8. The return of these fibres occurs chiefly at the periphery.

RESTORATION OF SENSIBILITY AFTER SECTION OF NERVES.—Arloing and Tripier showed that if all the nerves of an extremity in a dog are divided except one, the sensibility is retained to a greater or less extent throughout the whole limb. W. Mitchell (*Amer. Jour. of Med. Sc.* 1876, 321) finds that the same is true in the case of man. The sensibility in a limb with divided radial and median nerves, is rapidly restored, and that not by simple restitution and new formation of fibres, for the return of sensibility is observed before the motor portions of the nerves have united, as is shown by the muscular atrophy and the absence of reaction even to the strongest electrical stimuli. All the various qualities of sensation do not return to an equal degree; thus the sense of pain and touch may be almost normal, whilst that of temperature often remains quite destroyed, or at least highly disorganised.

Vaso-motor Nerves.

ON THE THERMAL EFFECTS OF OPERATIONS ON THE NERVOUS SYSTEM AND THEIR RELATION TO VASO-MOTOR NERVES.—A. Eulenburg, and L. Landois (*Virch. Arch.* LXVI. and LXVIII.), by means of Dutrochet's Thermo-Electric Elements and an Electro-Galvanometer, reinvestigated the effect of stimulation of the cervical sympathetic in its continuity in the rabbit, on the temp. of the ear on the same side. At once there was a cooling, which lasted 15—20 secs. longer than the stimulation, to be followed by an increase of temperature which exceeded the original value.

Sections of the cervical sympathetic produced at first a cooling of $\frac{1}{10}$—$\frac{2}{10}$° C., lasting only however 10 secs. and followed by a rapid increase of several degrees in the ear of the same side, whilst stimulation of the peripheral cut end caused the temp. to fall at once. In dogs slightly curarised the temperature of the foot gradually rose 2°—3° C. after division of the sciatic nerve; the temp. falls again however on stimulating the peripheral cut end, generally after a latent period of 15 secs. After a certain time the temp. does not sink any further, but gradually rises again. If the stimulus is again applied, the temp. again falls after a longer latent period, but to a less extent than by the first stimulation.

Eye.

"On Ophthalmoscopic Phenomena cited as Signs of Death." J. Gayat, *Ann. d'ocul.* LXXIII. 5 and *Centralblatt*, No. 45, 1876.——"An Optometer." Badal, *Ann. d'ocul.* LXXV. 101.——"On the reflex in the Region of the Macula." Brecht, *v. Gräfe's Arch.* XXI. 1.——"On the Field of Vision." Schneller, *v. Gräfe's Arch.* XXI. 133.

ON PHOTO-CHEMICAL PROCESSES IN THE RETINA.—Kühne communicated on January 5th to the *Natur-historisch-Medicinischer Verein*, of Heidelberg, a paper on the above subject.

A short time since, Boll (*Ber. d. k. Acad. zu Berlin*, 12. Nov. 1876) communicated to the Berlin Academy the remarkable fact that the external layer of the retina, *i.e.* the layer of rods and cones, possesses in all living animals a purple colour. During life, according to Boll, the peculiar colour of the retina is perpetually being destroyed by the light which penetrates the eye: darkness, however, restores the colour, which vanishes for ever almost immediately after death.

The wonderfully suggestive nature of Boll's discovery led Kühne to repeat his observations; in doing so, whilst he has confirmed the fundamental statement of Boll, he has ascertained a number of new facts of great interest.

Kühne's observations were made on the retinæ of frogs and rabbits. In the first place, implicitly relying upon the statements of Boll, he examined, as soon as possible after death, the retinæ of animals which had been kept for some time in darkness. He soon found that the beautiful purple colour persists after death, if the retina be not exposed to light; that the bleaching takes place so slowly in gas-light, that by its aid the retina can be prepared and the changes in its tint deliberately watched; that when illuminated with monochromatic sodium light, the purple colour does not disappear in from twenty-four to twenty-eight hours, even though decomposition have set in.

These first observations of Kühne on the vision-purple (Sehpurpur), as he terms it, whilst they showed that the disappearance of the colour is not, as Boll had asserted, a necessary concomitant of death, removed many of the difficulties which stood in the way of a careful investigation. Carrying out his preparations in a dark chamber illuminated by a sodium flame, Kühne was able to discover the conditions necessary to the destruction of the vision-purple as well as some facts relating to its restoration or renewal.

As long as the purple retina is kept in the dark or is illuminated only by yellow rays, it may be dried upon a glass plate without the tint changing; the colour is not destroyed by strong solution of ammonia, by saturated solution of common salt, or by maceration in glycerine for twenty-four hours. On the other hand, a temperature of 100°C. destroys the colour, and alcohol, glacial acetic acid, and strong solution of sodium hydrate produce the same effect.

Kühne's next observations were directed to the discovery of the influence of light of different colour upon the vision-purple. It would appear that the more refrangible rays of the spectrum have the greatest action, and that the red rays are as inactive as the yellow.

Kühne now found the incorrectness of Boll's assertion, that the retina of the living eye exposed to ordinary daylight does not exhibit the vision-purple, for on preparing the eyes of animals which had just been exposed to light, as rapidly as possible in the chamber illuminated by sodium light, he discovered that the retina was of a beautiful purple. It was only when eyes were exposed for a considerable time to the direct action of the sun's rays that a fading of the purple colour was perceived.

A most suggestive experiment now threw some light upon the

circumstances which retard the decolorisation, and which restore the vision-purple. The two recently extirpated eyes of a frog were taken; from one the retina was removed, whilst an equatorial section was made through the other eye, so as to expose the retina and still leave it *in situ*. Both preparations were exposed to diffuse daylight, until the isolated retina had lost its purple colour. On now taking the other preparation into the yellow chamber and removing the retina, it was found that its colour yet remained; it was *darkened*, but was bleached when exposed in its naked condition to daylight.

This experiment was confirmed by others, in which the effect of strong sunlight was substituted for that of diffuse daylight.

But the most curious results of Prof. Kühne's experiments have reference to the restoration of the vision-purple. If an equatorial section be made through a recently extirpated eye, and a flap of retina be lifted up from the underlying choroid and exposed to light, the purple colour of the flap will be destroyed, whilst the colour of the rest of the retina persists. If, however, the bleached portion of the flap be carefully replaced, so that it is again in contact with the inner surface of the choroid, complete restoration of the vision-purple occurs. This restoration is a function of the *living* choroid, probably of the living retinal epithelium (*i.e.* of the hexagonal pigment-cells, which used formerly to be described as a *part* of the choroid), and it appears to be independent of the black pigment which the retinal epithelium normally contains. As it is absolutely dependent upon the life of the structures which overlie the layer of rods and cones, it is natural that it should be observed to occur for a longer time after somatic death in the frog than in the rabbit.

Kühne's researches, though suggested by the interesting observation of Boll, have not only corrected many errors which that observer had committed, but have led to the discovery of facts which add immensely to the importance of the newly observed vision-purple.

They have shown that the living retina contains a substance which under the influence of light undergoes chemical changes, which vary in intensity according to the intensity and character of the luminous rays, and they point to the existence of structures in connection with the retina which as long as they are alive are able to provide fresh stores of substance sensitive to light.

Since the above account of Kühne's researches was written, he has published in the *Centralblatt* (1877, Nos. 3 and 4) a short paper, in which he announces the startling confirmation to his previous researches afforded by his having been able to obtain actual images on the retina which corresponded with objects which had been looked at during life.

The discoveries of Boll and Kühne must, as the latter remarks, have led to the thought that after all there might be some truth in the stories which we all have heard of things seen in death being left imprinted upon the eye. After his first researches Kühne endeavoured over and over again to observe on the retina of rabbits bleached spots corresponding to the images of external objects, but his endeavours failed. As Kühne remarks, and as all readers who

have understood his experiments will allow, in order to obtain a permanent photograph, or, as he terms it, *optogramme*, the effect of the light would have to be so prolonged or so intense as to destroy the balance between the destruction of the vision-purple and the power of the retinal epithelium to restore it.

Kühne took a coloured rabbit and fixed its head and one of its eye-balls at a distance of a metre and a half from an opening thirty centimetres square, in a window-shutter. The head was covered for five minutes by a black cloth, and then exposed for three minutes to a somewhat clouded midday sky. The rabbit was then instantly decapitated, the eye-ball which had been exposed was rapidly extirpated by the aid of yellow light, then opened, and instantly plunged in 5 per cent. solution of alum. Two minutes after death the second eye-ball, without removal from the head, was subjected to exactly the same processes as the first, viz. to a similar exposure to the same object, then extirpation, &c.

On the following morning the milk-white and now toughened retinæ of both eyes were carefully isolated, separated from the optic nerve, and turned: they then exhibited on a beautiful rose-red ground a nearly square sharp image with sharply-defined edges: the image in the first eye was somewhat roseate in hue, and less sharply defined than that in the second, which was perfectly white. The size of the images was somewhat greater than one square millimetre. [*Nature*, Feb. 1, 1877.]

On Daltonism and Young's Colour-Theory, and on Colour-Sensation.—E. Röhlmann (v. *Graefe's Arch.* xxii. p. 29), and J. Stilling, *Klin. Monatsch. f. Augenheilk.* xiv. July, 1876, and *Centralblatt*, No. 2, 1877.—Röhlmann investigated the sensibility of several cases of Daltonism for the different wave-lengths of the spectrum, and distinguishes three principal groups of disturbances of sensation. In the first group the violet end of the spectrum is shortened. In the second group the red end of the spectrum, and in the third both ends of the spectrum are shortened. For the two first groups, all qualitative visual impressions have to be made from the mixture of two primary colours, yellow and blue, whilst in the third group there is complete absence of the sense of colour.

According to Stilling acquired colour-blindness occurs in two forms, viz. as red-green blindness or as achromatopia, whilst blue-yellow blindness most probably never occurs at all. In the different forms of atrophy of the optic nerve, in amblyopia, also in many cases of neuro-retinitis acquired anomalies of the sense of colour often occur, whilst they do not occur in chorio-retinitis, glaucoma, apoplectic and albumenuric retinitis, or hæmorrhage into the macula.

On the action of Sulphate of Eserin on the Ciliary (accommodating) Muscle.—M. Reich (*Centralblatt*, No. 5, 1877) finds that this substance has an energetic action on the pupil, causing contraction sometimes even when calabar bean has failed. The effect lasts for 24 hours.

On the Chemistry of the Lens.—M. Laptschinsky (*Pflüger's Arch.* xiii. p. 631) analysed the lens of the ox, and finds that it has the following composition: Albumen 34·93 per cent.; Lecithin 0·23; Cholesterin 0·22; Fat 0·29; Soluble Salts 0·53; Insoluble 0·29; results which compared very closely to those obtained by Hoppe-Seyler. The quantity of albumen therefore present in the lens is greater than in any other organ. By rubbing up the lens with water and passing a stream of CO_2 through it a precipitate of globulin is obtained, which may be obtained by filtering. The fluid so separated gives no precipitate with acetic acid, and therefore contains no alkali-albuminate. It coagulates on heating, therefore contains soluble albumen, which seems to be identical with serum-albumen. The amount of cholesterin varies very much. In the yellow-coloured lenses of old people, more fat and less cholesterin was found.

Vascular System.

On the Chemical Conditions for the Origin of the Heart-beats, and on the Seat of Automatic Stimulation in the Frog's Heart.—Merunowicz (*Ludwig's Arbeiten*, 1875) has continued the series of researches begun in Ludwig's laboratory by Bowditch upon this subject. The usual teaching regarding the cause of the movements of the heart is that they are due to automatic motor ganglia placed within it, viz. Rémak's ganglia in the sinus venosus, and Bidder's ganglia in the auricular septum and the base of the ventricle. From the fact that the apex of the heart, when separated from the rest of that organ, ceases to beat, it has been almost universally believed that no ganglia are situate within it. Bowditch found that the apex separated from the rest of the heart under the influence of certain drugs could execute a series of more or less rhythmical movements. Merunowicz found that the apex of the frog's heart beat rhythmically for a long time if it was supplied with a mixture of defibrinated rabbit's blood, and 0·6 per cent. solution of Na Cl. The pulsations do not begin however for some considerable time, about an hour afterwards. The author concludes that the region of the apex of the heart as well as the ventricles and those parts immediately adjacent to the auriculo-ventricular sulcus also contain automatic organs for the production of heart-beats.

These experiments led Prof. Bernstein, of Halle (On the situation of the automatic organs in the frog's heart, *Centralblatt*, No. 22), to investigate this subject, and he gives strong reasons for dissenting from this view. He investigated whether under normal physiological conditions for nutrition, a spontaneous action of the automatic organs, said to exist within the ventricle, takes place. The ventricle of a living frog was compressed transversely by means of a pair of fine forceps, so that the continuity of the living tissue with the apex was thus destroyed. After removal of the compression the apex was distended with blood and remained at rest whilst the upper portion of the heart continued to pulsate, thus keeping up the circulation

through the injured portion of the heart and the body as shown by observation of the capillary circulation. The ventricle and its apex were therefore supplied with a sufficient amount of blood rich in oxygen; nevertheless the apex remained at rest. If the surface of the apex was slightly touched it contracted energetically, and was again filled by fresh blood: but even this produced no stimulating effect, and even after one to two days no recurrence of the pulsations was observed. Bernstein therefore believes that "under normal physiological conditions" no automatic stimulation occurs in the ventricle of the frog's heart.

The pulsations of the ventricle observed by Merunowicz under the influence of defibrinated rabbit-blood, are, according to Bernstein, not to be regarded as automatic, but are analogous to the action of any chemical stimulus, or such as are produced by a constant current. One must therefore regard defibrinated rabbit-blood as a chemical stimulus for the muscles of the heart of the frog. If this view of the matter is correct, a ganglionic system is not at all essential for the production of rhythmical movements in a muscular organ such as the heart. (Compare Foster and Dew-Smith, *Journal of Anatomy and Physiology*, x. 735.)

ON THE DEPENDENCE OF THE RHYTHM OF THE HEART ON VARIATIONS IN THE BLOOD-PRESSURE.—As to immediate effects of the blood-pressure on the rhythm of the heart, the results of previous investigators coincide tolerably well. They all found that when the blood-pressure was increased, after separation of the heart from the central nervous system, there was either acceleration or slowing of the heart-beats; and less frequently the heart beats unchanged. As to the interpretation of these phenomena, however, there is much variance. Indeed, Knoll and Nawrocki have even denied the "facts" of previous experimenters.

S. Tschiriew, of St Petersburg (*Centralblatt für die medicin. Wissenschaften*, No. 35), has again investigated this subject, and confirms the results of former experimenters (Ludwig, Thiry, Bezold, E. and M. Cyon). He has discovered a new fact, namely, a very considerable and sudden slowing of the heart-beats during the increase of the blood-pressure, as well after section of the cervical nerves alone as after complete separation of the heart from the central nervous system; a subsequent, sometimes very considerable, acceleration of the pulse after the cessation of increase of the blood-pressure, on cessation of the pressure exerted on the abdominal aorta.

The conclusions at which the author arrives are the following: 1. Considerable and rapid variations in the blood-pressure can change the rhythm of the isolated heart. 2. Every considerable and rapid increase of blood-pressure can directly excite both the inhibitory and the motor cardiac ganglia, by increasing or diminishing the number of beats, the number seldom remaining the same. 3. The final character of the changes in the heart's rhythm during the increase of the blood-pressure depends upon the counterbalancing actions of both of the above-named factors. For as a weak stimulation of the vagus can

completely extinguish the phenomenon of a maximal stimulation of the nervus accelerans (Bowditch), so it is easily understood, why (4) in those cases where the inhibitory mechanism of the heart is sufficiently developed and excitable, the increase of the blood-pressure for the most part slows the heart's rhythm, whereby the accumulated excitation of the motor ganglia appears after the cessation of the increase of pressure, *i.e.* as subsequent acceleration. If, on the contrary, the inhibitory apparatus is feebly developed and exhausted by previous stimulation, then a very considerable increase of the pulse-beats may occur during the increased blood-pressure. 5. The more pronounced the acceleration of the heart-beats during the increase of pressure, the feebler is the subsequent accelerating effect, and *vice versâ*. 6. The heart receives from the accelerating nervous system a constant tonic excitation. The central ends of this system can be excited by increase of the blood-pressure, but not by its diminution. In the normal condition, in addition to this direct influence, there is an indirect one, through the vagi and accelerantes. 7. Small doses of atropin paralyse the peripheral ends of the vagi (a fact already well known), but not the inhibitory apparatus itself. 8. The pulsus bigeminus is simply a slow pulse, in which the ventricle is peristaltically contracted. 9. Anacrotism of the pulse, as is the case in aortic insufficiency, or in the arterial sclerosis, is the expression of peristaltic heart-contractions, and not of variations in the elasticity of the wall of the vessel.

ON THE EFFECT OF BATHS ON THE BLOOD-PRESSURE.—F. Rewnoow (*Centralblatt*, No. 50) observed that on curarised dogs baths of 30—35° C. had little effect on the blood-pressure; above 35°, after a rapid but temporary increase, they caused a fall in pressure. If the animal after the bath (35° and above) was allowed to remain at the temperature of the room, or was douched with cold water, the blood-pressure rose, and was followed by a fall, which was more pronounced the lower the temperature of the cold water and the higher that of the bath. Baths under 30° increase the pressure until the body-temperature begins to fall. A continuous increase of the body-temperature in baths above 35° C. increases the pressure. Division of the vagi does not affect the action of the baths, but section of the cord at the second cervical vertebra caused a fall, which was not affected either by the baths or douche. The author concludes that by the baths and douches the cutaneous sensory nerves reflexly affect the vasomotor centres to produce the changes in the blood-pressure.

THE VOLUMETRIC ESTIMATION OF THE BLOOD-PRESSURE IN MAN.—S. von Basch (*Wiener Med. Jahrb.* 1876, 4), with the aid of Mosso's plethysmograph, investigated the changes in volume of the passive arm during complete rest of the body; here there were long unequal waves, which corresponded to a rhythmical increase and decrease of the arm. The individual experimented on was placed in the horizontal position in bed, and even slept without the long waves undergoing a change.

These waves cannot, as Mosso imagined, be ascribed to contractions of the vessels, but rather to changes in the tension within the aorta, for a synchronous pallor and congestion analogous to the waves were not observed. These waves seem to the author to correspond to the well-known curves of Traube and Hering.

Curves taken during sleep showed at the beginning of sleep a pronounced sinking of the curve, which, however, did not last longer than a minute to give place to the above Traube-Hering curves. This sinking he refers to an affection of the vaso-motor centre, the blood of the aorta fills specially the abdominal organs, the pressure within the aorta falls, and therewith occurs the diminution in the volume of the arm.

During mental activity—from experiments made upon physicians—B., in opposition to Mosso, finds no change in the volume of the arm, at least no diminution in its volume was observed.

The author investigated the condition of the volume of the arm when the vascular area of the splanchnic was considerably diminished by compression of the abdomen, thus offering considerable resistance to the outflow of blood from the aorta. If this compression of the abdomen is comparable to stimulation of the splanchnic, there must be an increase in the volume of the arm, which is actually the case. The same effect is produced by muscular action of the abdominal walls compressing the abdomen. The converse effect, viz. diminution of the volume of the arm, is produced by diminution of the intra-abdominal pressure. According to Schatz this may be produced by raising the arms above the head, thus raising the ribs by the action of the pectoralis major. In B.'s experiments this was always followed by a diminution in the volume of the arm. The experiments show that one may conclude as to an increase or diminution of the arterial blood-pressure from an increase or decrease in the volume of the arm.

An Inquiry into the Cause of the Slow Pulse in Jaundice.—J. Wickham Legg (*Proc. Roy. Soc.* 1876, No. 69) finds that the salts of the bile-acids slow the beat of the excised frog's heart (Bowditch's preparation), even after the addition of atropin to the serum contained in the heart. If atropin was added after the action of the bile-acid salts there was no effect. The same was observed on the intact frog, when, after previous administration of atropin, a 10 per cent. solution of the bile-salts was dropped upon the heart. The vagus therefore does not seem to be implicated in the slowing of the pulse. The muscle-paralysing properties of the bile-salts, observed by Ranke on the injection of a 1 per cent. solution into the muscular arteries, are, according to the author, not a specific action, but depend upon coagulation of the albumen, which also occurs outside the body with such a concentration. The introduction of 0·3 grms. of the salts into the lymph-sac of a frog does not alter the muscle-curve. Even the cardiac muscles do not seem to be affected by these salts. The curve obtained from a Luciani heart-preparation remained unchanged when a 1 per cent. solution of the salts was added to the serum. By

exclusion the auther seeks to prove that the cause of the slowing of the pulse by bile-salts, *i.e.* in icterus, is to be sought for in the motor ganglia of the heart itself, a view announced by Röhrig thirteen years ago, though on less substantial experimental evidence.

ON THE ORIGIN OF FIBRIN, AND ON THE CAUSE OF THE COAGULATION OF THE BLOOD.—P. Mantegazza's (*Moleschott's Unters. zur Naturl.* XI. p. 523, and *Centralblatt*, 1877) investigations differ from those of other experimenters in as far as they refer to observations made on living animals. The author, like Schmidt, ascribes an important rôle in the coagulation of the blood to the colourless blood-corpuscles, with this difference, however, that Schmidt explains the formation of fibrino-plastic substance as a phenomenon accompanying the death of the blood, whilst the author regards it as a vital effect, as a kind of reactionary phenomenon, in consequence of a stimulus, which consists most frequently in their contact with foreign matter. The process ends with the death and the passage of the colourless corpuscles into the clot. In support of this view we have (1) a large number of experiments, which show that coagulation always takes place within the blood-vessels when the wall of the blood-vessel is changed, *e.g.* by irritation or burning. The injured spot is always covered with heaps of colourless blood-corpuscles sticking together, and around the whole the fibrin is deposited. The same also occurs when a foreign body with a rough surface is introduced into the lumen. (2) The fact, that all fluids capable of coagulation contain colourless cells. The author quotes Beale as his precursor in this matter, though he does not seem to be acquainted with the experiments of Lister and Zahn on this subject. He does not decide definitely whether the fibrin proceeds from fibrinogen and fibrino-plastin, though he leads one to believe that he adopts this view, and regards the production of fibrino-plastin as due to stimulation of the colourless corpuscles.

The differences between the blood of the jugular and splenic veins, and the connection between the number of red blood-corpuscles, and the quantity of fibrin contained in the blood, are discussed. The results are (1) The differences between the two kinds of blood (jugular and splenic veins) in fibrin, and number of corpuscles are inconstant in the dog. (2) After the injection of urea into the veins, the number of blood-corpuscles diminishes rapidly and considerably, and the amount of fibrin obtained from the blood increases. With 4 grm. urea, the number of blood-corpuscles in 1 cc. sank within four days to 1,250,000, and the fibrin rose from 2·628 to 8·089 per thousand. As a maximum 19 per thousand was obtained. The action of urea is more pronounced in herbivora than in dogs, and does not take place outside the body. (3) Lactic acid has a similar effect on the fibrin and corpuscles, but the effect is much more complicated. The author refutes Beltrami's theory, that the fibrin is the "detritus of the muscle-substance." In three cases of tetanus, Mantegazza observed 4,8 —2,7—1·6 per thousand of fibrin, *i.e.* rather a diminution than an increase in the fibrin. Other objections are cited in the original.

On the Relation of Chloride of Sodium to certain Organic Fermentative Processes.—A. Schmidt, *Pflüger's Arch.* XIII.

I. The coagulation of milk by rennet. If an extract of the mucous membrane of the stomach of the calf (prepared by ·25 per cent. hydrochloric acid) be by dialysis freed from all soluble salts, and if milk be similarly freed, then if the two fluids be mixed (at 17 Cent. = 62·6 Fahr.), the coagulation, *i.e.* the separation of casein, takes place at once, at a somewhat lower temperature (15 Cent. = 59 Fahr.) in 25 seconds. It is therefore clear that the soluble salts, and, above all, common salt, delay and prevent the coagulation of milk by rennet.

II. The digestion of albuminous bodies by pepsin and hydrochloric acid. Coagulated albumen, freed by dialysis from its salts, is much more easily dissolved by the gastric juice than the fibrin (even when swollen up) usually employed. Even the albumen, coagulated by heat and separated in flakes from diluted egg-albumen, is dissolved more rapidly than the albumen coagulated within the shell of the egg. In this case, it does not depend alone upon the form in which the albumen is excreted, though this is more favourable in the former case, but essentially upon the amount of salts present. For, if the solid coagulated albumen be rubbed down finely with water, it is still more difficult to digest, and the easy digestibility of the flocculent albumen may be set aside by the addition of a small quantity of chloride of sodium. The addition of 0·5 to 0·6 per cent. of chloride of sodium to a digestive fluid poor in salts, increases the time required for digestion from 3 to 10 times. Solutions of peptones are only precipitated by tannic acid in the presence of salts; and the amount of pepsin in the stomach of newly-born animals is small, but not absent, as indicated by Hammarsten.

III. The coagulation of fibrin. The author has already shown that the amount of fibrin obtainable from a fluid increases, *cæteris paribus*, within certain limits, with the amount of fibrino-plastic substance contained in it, but beyond these limits it diminishes. The same is true for the quantity of the salts in the fluid. The simplest experiment to show this is to dilute blood-plasma with water. From the diluted plasma less fibrin is excreted than from the undiluted, but the amount increases with the addition of chloride of sodium; and when the amount of chloride of sodium in the diluted fluid reaches 1 per cent., the amount of fibrin excreted is almost as great as in normal plasma. With 2 to 2·5 per cent. the amount is much less; and if still more chloride of sodium be added, the plasma remains fluid. In these and all other experiments on coagulation, a small quantity of a solution of hæmoglobin was added. The time of coagulation is thereby very much shortened, and a resolution of the fibrin does not take place, which, without the addition of hæmoglobin, is often the case. The addition of chloride of sodium, however, never causes coagulation in a fluid, which by the addition of fibrin-ferment alone does not coagulate. It therefore seems, from these and the author's former experiments, that the amount of fibrin obtainable from a fluid depends upon several conditions: (1) The

amount of the fibrin-regenerators; (2) Quantity of the salts; (3) Amount of alkalinity; (4) Temperature. The influence of the quantity of ferment and that of hæmoglobin, on the amount, is still doubtful. What now happens when the fibrin-factors and the ferment are brought together without the presence of the salts? For these experiments, the blood-plasma of a horse was filtered in the cold, treated with 0·5 per cent. of soda, and then subjected to dialysis. The addition of soda was necessary in order to prevent the coagulation during the dialysis. In such solution, freed from salts, on the addition of the fibrin ferment there is formed a product insoluble in water, and only soluble in an excess of alkali. It is not fibrin, but in the presence of neutral salts in an alkaline solution it becomes fibrin. If no excess of alkali is present, the whole of the globulin-like substances contained in the fluid, even to traces, pass into this product, so that, on diluting the filtrate with water, and passing a stream of carbonic acid through it, only a slight opalescence is obtained. Concentrated salt solution, previously added to fluids capable of coagulating, prevents this entirely, while the alkaline solution of the above-named product is at once precipitated by concentrated solution of chloride of sodium. But the fibrin so precipitated differs from ordinary fibrin. If soda (·002 to ·003 per cent.) be added to the blood-plasma just before coagulation, the fluid becomes changed into a thick slimy tenacious mass. (*Lond. Med. Rec.*, Jan. 1877.)

On the Ash of Blood.—A. Jarisch (*Oesterr. med. Jahrb.* 1876, Hft. 1), gives the following as the mean. In the case of the human blood it was obtained by venesection.

	Man—normal.	Horse.	Dog.
Phosphoric acid anhydrous ...	8·82	8·38	12·74
Sulphuric acid anhydrous	7·11	6·31	4·13
Chlorine	30·74	28·63	32·47
Potash	26·55	29·43	3·96
Soda	24·11	21·15	43·40
Lime	0·9	1·08	1·29
Magnesia	0·53	0·60	0·68
Oxide of Iron	8·16	9·52	8·64
		CO_2 1·30	

On the Decomposition of Urea in the Blood.—V. Istomin (*Petersb. Med. Wochensch.* 1876, No. 25, and *Centralblatt*, No. 5, 1877).
——"On the Quantitative Estimation of Albumen in Blood-Serum."

J. Puls (*Pflüger's Arch.* and *Centralblatt*, No. 51, 1876).——"On the Dissociation of Bicarbonate of Soda at a temperature of 100°." V. Urbain, *Comptes rendus*, LXXXIII. No. 10.——"The effect of Purgation and Inanition on the number of Blood-Corpuscles." Brouardel, *Union Méd.* 1876, No. 110, *Centralblatt*, No. 48.

ON THE PROCESS OF OXYDATION IN NORMAL AND ASPHYXIATED BLOOD.—N. Stroganoff (*Pflüger's Archiv*, Band XII., *Centralblatt für die Medicinischen Wissenschaften*, No. 28) has endeavoured to decide the question:—1. *Whether the Blood of an Asphyxiated Animal still contained Oxyhæmoglobin.*—He placed between two glass plates the completely isolated jugular vein, or the carotid, of rabbits, and so compressed them that a spectroscopic investigation was possible. The vessel was protected from contact with the air. It was invariably found that the blood, even at the last moment of the last cardiac contraction, always contained oxyhæmoglobin.

2. *On the Amount of Oxygen in the Lungs during Asphyxia.*—The composition of the air of a closed space in which the animal, in consequence of want of oxygen (the CO_2 was absorbed), was asphyxiated, was estimated when the respiratory movements ceased. As the mean of four experiments, the amount of oxygen in the air at this moment was 3·54 per cent., agreeing well with previous results. If one assume, that the blood had absorbed the same amount of oxygen from this air as in normal respiration, then the amount of oxygen in the air within the lungs would be 2·73. The complete cessation of all respiratory movements is regarded by the author as the second stage, and at once the air still remaining in the lungs was extracted by means of a mercurial air-pump. The analysis gave as the mean for the oxygen of this air 2·337. If the air was taken from the lungs after cessation of the movements of the heart, the amount of oxygen was only 0·403 per cent.; almost all the oxygen, just to a trace, was absorbed by the blood.

3. *On the Capacity of Asphyxiated Blood to absorb the last Traces of Oxygen from the Air in the Lungs.*—Asphyxiated blood, taken from an animal after cessation of the respiratory movements, was shaken with a quantity of air very poor in oxygen, and then its composition ascertained. It was shown that the blood absorbs oxygen, even when the latter is only present to the amount of 1 per cent. or less. To determine whether this is also true of the lungs, Stroganoff pumped out the air from the lungs after cessation of the respiratory movements, and introduced air of known composition instead. Here also oxygen disappeared from the air. The amount of oxygen introduced with the air, in one case was 1·289 cubic centimètres; the remainder 0·747. The blood in the lungs therefore absorbs oxygen from the air in the lungs, even after cessation of the respiratory movements, so that not a trace of oxygen is left.

4. *On the Extent of the Oxydation Process in Normal and Asphyxiated Blood.*—In order to estimate this in asphyxiated blood, it was shaken with a sufficient quantity of atmospheric air, and the amount of oxygen remaining and that of hæmoglobin determined.

If the amount of oxygen absorbed is greater than corresponds to the quantity of hæmoglobin, then oxygen must have been used for the oxydation of reducing substances in the blood. As asphyxiated blood is never quite free from oxygen—according to Pflüger, 1·75 volume per cent.—this also must be taken into consideration. The experiments were repeated in the same way with arterial and venous blood. Even arterial blood absorbs oxygen, as Pflüger had already shown, to the extent of 1·066 to 1·295 cubic centimètres for 100 cubic centimètres. Stroganoff assumes that the blood, in virtue of its hæmoglobin, is completely saturated with oxygen. The asphyxiated blood invariably absorbs considerably more oxygen than corresponds to its amount of hæmoglobin, to the extent of 4·93, 2·84, 3·31, and 2·34 cubic centimètres for 100 cubic centimètres of blood. If one assume the amount of oxygen contained in it as = 1·75 volume per cent., we have the mean 5·10 volumes per cent. as the expression of the reducing substances present in the blood. The author then deducts the amount of oxygen required by the blood for the oxydation = 1·18 cubic centimètres, and arrives at the number 3·927 cubic centimètres of oxygen. For all the details and data of the experiments we must refer to the original.

Graphic Investigations on the Heart-beat under Normal and Diseased Conditions.—L. Landois (*Berlin*, 1876, 8vo. pp. 93) has studied the movements of the air in the air passages by means of sensitive flames. *Vide* also *Centralblatt*, No. 5.——"On Polygraphs." Grunmach, *Berlin. klin. Wochenschr.*, No. 33, 1876.

On the Relation of the Vagus to the Accelerans.—N. Baxt (*Ludwig's Arbeiten*, 1875) has performed a very elaborate and extended series of experiments on these two nerves, both nerves being irritated simultaneously. He does not regard them as strictly antagonistic to each other in their action; for stimulation of the vagus was not prevented by simultaneous stimulation of the accelerating nerves. It is well known that the effect of stimulation of the vagus upon the heart only lasts for a very short time, the heart being slowed or arrested in its action, but may begin to beat even while the stimulation of the vagus is continued. Baxt finds that stimulation of the accelerans however, on the contrary, has a prolonged effect on the action of the heart.

"On the Physiology of the Vagus." O. Rosenbach, *Centralblatt*, No. 5, 1877.——"On the effect of Stimulation of the Splanchnicus on the Blood-pressure without its own vascular area." S. v. Basch, *Ludwig's Arbeiten*, 1875.

On the Difference in the Action of the two Vagi.—L. Tripier and Arloing (*Gaz. des Hôpitaux*, Dec. 14, 1876) assert that the right vagus acts more energetically on the heart [a circumstance already well known] than the left one, and that the reverse is the case with the lung.

Section of one vagus may cause death in the ass, rabbit, and horse, and section of the right vagus produces this result oftener than the section of the left.

M. Philippeau found the following as the result of section of the vagi. If in a rat one vagus is divided, and thirty-one days afterwards the other is cut, the animal lives. If the second vagus is cut before the expiring of thirty-one days, it dies. In order that a dog may survive, an interval of sixty days must elapse between the sections of the vagi; and in the guinea-pig twenty-four days.

Respiratory System.

"Influence of CO_2 on the Respiration of Animals." F. N. Raoult, *Comptes rendus*, LXXXII. No. 19, and *Centralblatt*, No. 44.——"On the Respiration of the Fœtus." Zweifel, *Arch. f. Gynäkol.*, IX. 291.——"On the Crystalline Constituents of the Lung Juice." G. Grübler, *Ludwig's Arbeiten*, 1875.——"On the Theory of the Intercostal Muscles." A. W. Volkmann, *Zeitsch. f. Anat. u. Entwicklungsg.*, II. 159, and *Centralblatt*, No. 6, 1877.

Effect of the Respiration on the Blood-pressure.—A. Stefani (*Communic. fatta al* XII. *Congr. degli Scienziati in Palermo*, 1875, and *Centralblatt*, No. 53) kept up artificial respiration in curarised dogs and took a carotid tracing in the ordinary way. If the artificial respiration was suddenly interrupted, there was always a considerable increase of the blood-pressure (110 to 194 mm. Hg.), which did not always occur immediately after interruption of the respiration, but a shorter or longer interval always elapsed before it took place. This difference Schiff showed depends upon the amount of O. present in the blood at the moment the respiration is interrupted; the increase of the blood-pressure occurring later the more O. is present in the blood, and *vice versâ*.

Analysis of the blood-curve shows that the increase of the blood-pressure must not be expressed by a straight line rising steeply, but by a wavy one. This fact is of importance as showing that variations in the blood-pressure can take place independently of every mechanical action of the respiration. Further it is shown that with increase of the blood-pressure the number of pulse-beats is diminished, whilst the individual pulse-beats are more extended. This depends upon a stimulation of the vagus centre, for it no longer occurs when the vagi are divided. If the interrupted respiration is again commenced, the blood-pressure falls to its original level, and the original number of beats and extent of heart-beats are restored.

The author explains these phenomena in accordance with the view of Schiff on the cause of the respiratory oscillations in the blood-pressure. He repeated his experiments on dogs, in which, according to A. von Bezold, the vaso-motor centre was paralysed by division of the spinal cord. Like other observers he always found a fall of the blood-pressure after this operation. If now the artificial respiration was interrupted, the blood-pressure rose after a time considerably, whilst the heart-beats became simultaneously less frequent but more extended. But this increase of the blood-pressure is never so great as in animals with intact nervous system. It may even be absent if

the vagi are not divided at the same time as the cord. If this is the case, however, one always has an increase of the blood-pressure, but without any simultaneous change in the number or extent of the pulsations.

From this it appears that the increase in the blood-pressure after interruption of the artificial respiration is independent of the action of the vaso-motor centre, but still, however, not nearly to the extent which occurs when this centre is in action. We may therefore suppose that after interrupting the respiration the products of the chemical changes occurring in the blood, besides acting on the vaso-motor centre in the medulla, also act directly on the ganglia of the heart. The author has convinced himself by central experiments that the small vaso-motor centres which, according to Nussbaum and Goltz, exist in the cord, have no effect on the above phenomenon. The centre for the innervation of the heart, and which is placed in the medulla, was also eliminated by dividing both vagi and sympathetics in the neck. Even in these animals an increase of the blood-pressure took place after interruption of the artificial respiration; one can only conclude therefore that the ganglia in the heart itself are excited by the changes in the blood.

Lastly, the author points out the importance of artificial respi ration in recent cases of apoplexy, by assisting on the one hand in diminishing the pressure on the respiratory centre, and on the other by diminishing the blood-pressure, and thus preventing a further escape of blood.

Digestive System.

Alimentary Canal.

"On the action of Alkalies on the Diastatic action of Saliva and Pancreatic Juice." Cornillon and Bretet, *Progrès Méd.* 1876, No. 7, and *Centralblatt*, No. 47, 1876.——"On Peptones." A. Kossel, *Pflüger's Arch.* XIII. p. 309, and *Centralblatt*, No. 1, 1877.——"Physiological and Microscopical Investigations on the Excretion of Pepsin." G. Herrendörfer, *Diss.* Königsberg, 1875, finds that although the first three stomachs of ruminantia contain no glandular elements, they still have digestive properties. This is most easily explained by the infiltration theory, from the gastric juice passing in and the mucous membrane absorbing and retaining the pepsin. Vide *Centralblatt*, No. 42, 1876.——"Synthesis of Fat." A. Perewoznikow, *Centralblatt*, No. 48, 1876.——"On the Synthesis of Albumenoids in the Animal Organism." Rudzki, *Centralblatt*, No. 50.——"On Emulsions and their value for the absorption of Neutral Fats in the small Intestines." J. Steiner, *Reichert and du Bois' Arch.* 1874, 286. *Centralblatt*, No. 50, 1876.

On the Formation and Excretion of Pepsin in Batrachians.—H. v. Swizcicki (*Pflüger's Arch.* XIII. p. 442) experimented chiefly on frogs, and used Grützner's coloured fibrin method. He finds that by far the greatest amount of pepsin is derived from the œsophagus.

The amount varies with the condition of the gland-cells of the œsophagus. During digestion the cells were large and contained much pepsin; during hunger they were small and contained little pepsin. The amount of pepsin extracted from the stomach was much less, as compared with that from the œsophagus. The amount of pepsin in the œsophagus and stomach increases in the first 6—10 hours after food, then falls towards the 20th to a minimum. The formation of acid takes place where 'Belegzellen' are present.

On Organised and so-called Amorphous Ferments and on Trypsin (Euzym of the Pancreas).—W. Kühne (*Verhand. d. Naturh. Vereins zu Heidelberg*, Neue Folge, Band I. p. 194, and *Centralblatt*, No. 36) proposes to call the amorphous ferment euzym, the ferment of the pancreas, trypsin. Its action is not arrested by salicylic acid, and this substance is very applicable for demonstrating the specific digestive actions of the pancreas from other actions, such as putrefaction, which may occur simultaneously. Eight hundred grammes pancreas of ox treated with four grammes salicylic acid and two litres of water at 40° Cent. showed no bacteria, no smell of indol, whilst the glands were dissolved after several hours. Filtered portions digested powerfully. Sulphuric acid and hydrochloric acid in equal quantity did not produce the same effect, but acetic acid did so in a striking manner. Salicylic acid does not affect the action of pepsin, but rather protects its solutions from putrefaction. Pepsin destroys the action of trypsin, but the pancreas ferment does not affect pepsin, but this latter is rendered inactive by an alkaline reaction. The explanation offered by Kühne of the increased appetite of dogs with biliary fistula is, that normally the pepsin is destroyed by the bile. If the bile is not poured out, the pepsin still active passes into the duodenum, and disturbs the pancreas-digestion.

According to Heidenhain the pancreas contains only zymogen. If, however, according to Kühne, a pancreas quite fresh and still warm is rubbed up with absolute alcohol, and from the gland so treated, a watery extract is prepared at 0° C. (32° Fahr.), this extract is at once active. Heidenhain's zymogen is therefore a body capable of being split up by alcohol. If the extract of the gland is repeatedly precipitated by alcohol and dissolved in water, and if to the watery solution acetic acid is added to 1 per cent., then an albuminous body is precipitated, which the author terms *leukoid*, whilst the filtrate again precipitated by alcohol yields a precipitate essentially consisting of trypsin. Trypsin is amorphous, transparent, of a feeble straw-yellow colour, easily soluble in water. The solution, even when rendered alkaline, can be kept unchanged, no formation of peptones, leucin, or tyrosin taking place. On being boiled, it is decomposed into coagulable albumen and peptone. In watery solution, trypsin dissolves fibrin when warmed almost at once; the solution contains peptone, antipeptone, leucin, and tyrosin. The process is this: first peptone is formed, which is not to be distinguished from that formed in the stomach, and this now produces anti-

peptone and the other substances, which are chiefly products of decomposition and crystalline.

Trypsin has no action on starch and dextrin; putrid albumen and bacteria contain no trypsin, and, in fact, no ferment which resists the action of alcohol. No trypsin is to be found in arterial blood, the salivary glands, and lymph glands of the mesentery.

P. Grützner (*Pflüger's Archiv*, Band XII. p. 285) has also made some observations on the amorphous ferments.

1. The salivary glands of the dog, according to this author, do not form any sugar ferment. It is true that, with long digestion of the mixed saliva or the glycerine extract of the glands with starch mucilage, a sugar reaction is obtained; such traces of a diastatic ferment, however, are found in all parts of the body. The salivary glands of man and of the vegetable feeders undoubtedly contain a diastatic ferment; in the rabbit the parotid is much richer in ferment than the submaxillary gland.

2. The use of Brunner's glands in the wall of the intestine has long been doubtful. The author finds that their gland cells are microscopically not to be distinguished from those of the pyloric glands; in fact, by treating them with glycerine or hydrochloric acid of 1 per cent., an extract containing pepsin may be obtained, which is richer in pepsin when the cells are large and clear than when they appear turbid. Whether the ferment secreted by these glands is active during life is, from the alkaline reaction in the intestine, doubtful. No diastatic ferment was to be detected in Brunner's glands.

3. The amount of the diastatic ferment in the pancreas varies with the time which has elapsed since the last meal. It is least six hours after food, and greatest fourteen hours thereafter. The quantity of the ferment was estimated by the action of the glycerine extract (10 grammes fresh pancreas and 100 grammes glycerine) on starch mucilage, analogous to the method of Grünhagen for estimating the amount of pepsin. The starch mucilage was placed in a filter, and was treated with an equal amount of the glycerine extract (0·3 gramme); the quantity of the filtrate produced in a given time gave the measure of the activity of the extract. The first filtrates produced by the action of the diastatic ferment were rich in erythrodextrin (Brücke), poor in sugar, whilst the latter contained much more sugar. Further experiments led to the general result, that the products vary according to the intensity of the action of the ferment. The smaller the amount of ferment and the shorter its action, the greater the prevalence of the dextrin; in the opposite case, the sugar. The same is true for pepsin. With a small amount of the ferment, short time of action, etc., syntonine is the chief product formed; in other cases, peptone. Carbonate of soda of 0·5—1 per cent. arrests the action of pepsin. In all cases, the intermediate products dextrin and syntonine (parapeptone) are chiefly formed. These observations, together with many others, prove that the amorphous ferments are destroyed during their action. The pancreas ferment which acts upon the fats presented great difficulties

in its investigation. It is very unstable in its nature. The glycerine extracts of the pancreas gradually become acid, and as soon as this takes place the fat-decomposing action ceases. Later, the author employed a feebly alkaline glycerine. The glands were poorest in fat ferment six hours after an ample meal, and the quantity rose till the fortieth hour. The fat ferment is only active in an alkaline or neutral solution. Even the salivary glands yield far more active extracts when they have been exposed for some time to the air, than when they are prepared quite fresh. Similar observations have been made by Liversidge and Heidenhain for the pancreas; by Von Wittich, Ebstein and Müller for the liver; and by Hammarsten for the ferment of the stomach.

ON PANCREATIC DIGESTION.—G. Weiss working under Salkowski (*Virch. Archiv*, LXVIII. 413) found zymogen only in four cases out of 16 (dogs), whilst in the other twelve the first extract was not less active than the second. In six cases the glands were inactive. This is to be explained by the rapidity with which the zymogen undergoes a change under the action of O. The pancreas of human subjects was found to be quite inert.

Liver.

ON LYMPHATICS OF THE LIVER.—A. Budge (*Ludwig's Arbeiten*, Band x.) from his injection experiments draws the following conclusions regarding the perivascular spaces of the liver. A closed system of lymphatics exists in the liver, and is in most intimate relation to the venous blood-vessels. Within the lobules there are simple lymphatic sheaths around the blood-capillaries, which prevent the direct contact of the hepatic cells with the blood, so that any exchange between these can only take place through the medium of the lymph. Just as the blood-capillaries at the margin of the lobules unite into larger trunks, so the lymph-sheaths pass into lymphatics, which are placed in the walls of the veins, and by means of the interlobular vessels pour their contents upwards into the lymphatics of the diaphragm, and downwards into those of the hilus.

ON THE RELATION BETWEEN THE QUANTITY OF ALBUMEN TAKEN IN THE FOOD, AND THE SULPHUR EXCRETED IN THE BILE.—Kunkel (*Ludwig's Arbeiten*, 1875) collected the bile during the whole period of the experiment in caoutchouc bags. Of course, on account of the low pressure under which the bile is excreted, care must be taken that there be no resistance to its outflow. The experiments were performed upon dogs.

In the first series of experiments, coagulated lamb's and calf's blood was the nutriment. In five days the amount of sulphur taken with the blood was 3·245 grammes; excreted by the bile 0·615, and by the fæces 0·670. But as after the exclusion of the bile-duct, the sulphur in the fæces must essentially be derived from the undigested albumen, the 0·67 must be deducted from the sulphur of the food; 2·575 grammes were therefore absorbed of which 0·615 was excreted

by the bile, 23·8 per cent. This number is, however, too high, as the animal had lost 460 grammes-weight, i.e. besides the food, had also used up other bodies containing sulphur.

In the second series, where flesh was given as the food, 14·7 per cent. sulphur was excreted in the bile; in the third series 17·3 per cent. By taking the individual days, it appears that the amount of sulphur excreted in the bile, relatively to that of the food, continually increases. In the second series, the percentage on the second day was 9·2: then 7·7, 9·6, 12·7, 21·3, 30·2. In the third series, it was 13·1, 19·3—24·6. As the amount of food taken during the latter days of the second series was much less than at the early period of the experiment, it follows that the increase of sulphur excreted by the bile does not occur on the same day as the albumen is supplied, but considerably later. Similar relations hold for the sulphur of the urine.—[*Lond. Med. Rec.* Jan. 1877.]

Glycogen.

"On the action of warm Solutions of Potash on Glycogen." M. v. Vintschgau and M. J. Dietl, *Pflüger's Arch.* XIII. 253, and *Centralblatt*, No. 51.——"On Sugar-producing Ferments in the Animal Organism." M. Abeles, *Wiener med. Jahrb.* 1876.——"On the action of Acids and Alkalies on the Liver Ferment." W. Ebstein and J. Müller, *Ber. d. deutsch. chem. Ges.* VIII. 674.——"On Glycogen and Glycocoll in the Muscles of Pecten Inodians." N. H. Chittenden (*Annal. d. Chem. et Pharm.* CLXXVIII. 266) found the amount of the former to be 1·98 to 2·43 per cent.; of the latter 0·39—0·71, which substance up to this time had not been found in the animal economy.

On the Conversion of Glycogen into Grape-Sugar by Saliva and Pancreatic Juice.—Seegen (*Centralblatt*, No. 48) remarks that in all physiological text-books these two secretions are said to transform glycogen rapidly and completely into grape-sugar. The author finds that this is not the case, even though the glycogen is obtained in various ways. The mixture of glycogen and the ferment was allowed to stand for twenty-four hours; still the solution, after complete fermentation, contained only a fraction of the grape-sugar which ought to have been formed if the whole amount of glycogen dissolved had been transformed into grape-sugar. The amount of sugar present varied; when saliva was the ferment employed, it varied from 34 to 41 per cent.; if the pancreas extract were employed, it was 45 to 48 per cent.—*Lond. Med. Rec.* Jan. 1877.

On the Effect of Ligature of the Artery and Section of the Nerve on the quantity of Glycogen in Muscle.—Th. Chandelon (*Pflüger's Arch.* XIII. p. 626) ligatured the common iliac artery on one side of a rabbit, and after 17—24 hours estimated the amount of glycogen in the muscles. Regularly there was a diminution of the glycogen (from 37 to 77 per cent.) on the ligatured side in comparison with the sound one. The author explains this decrease by the diminished supply of glycogen or by its more scanty formation

in the badly nourished muscle. The diminution after ligature is greater than that produced by tetanisation of the muscles. If the sciatic nerve is divided the amount of glycogen on the side operated on is always increased from 5—17·2 per cent. The increase of glycogen is ascribed by the author to the disappearance of muscular activity, which very probably is connected with the using up of glycogen when the glycogen is formed as under normal conditions.

On the Influence of certain substances on the Glycogen of the Liver.—N. Konjkoff (*Diss.* Petersburg, 1876, p. 36, and *Centralblatt*, No. 42) comes to the following conclusions: (1) In the normal liver taken from a living rabbit there is none or only traces of sugar. (2) Nearly all glycogen disappears from the liver of a rabbit after starving it for four days. (3) The introduction of cane and grape-sugar into a rabbit's stomach causes, even within 6—8 hours, a considerable increase of glycogen in the liver. (4) This is not the case on giving an equal quantity of mannite. (5) Arsenious acid mixed with the food produces, in large poisonous doses, complete disappearance, and in small doses considerable diminution, of the liver glycogen. (6) The simultaneous introduction of sugar and arsenious acid causes an increase of glycogen. (7) Amyl nitrite and nitro-benzin act like arsenious acid. (8) The simultaneous introduction of grape-sugar and amyl nitrite produces no increase in the liver glycogen. (9) It is probable that the glycosuria caused by amyl nitrite has a relation to the above.

On Human Liver Glycogen.—E. Kulz (*Pflüger's Arch.* xiii. 267) obtained from ten parts of liver of a diabetic patient, besides sugar, 0·685 grm. glycogen, although the *sectio* was made 12 hours after death, and the last meal was taken 34 hours before death. The glycogen showed the normal characters. The sugar obtained by boiling it with dilute HCl. rotated the polarized ray to the right, and was capable of fermentation.

On the Effect of Ligature of the Bile-duct on the Amount of Glycogen of the Liver. E. Kulz and E. Frerichs (*Pflüger's Arch.* xiii. 460, and *Centralblatt*, No. 55).—In guinea-pigs the amount of glycogen, after this operation, was 0·088, 0·1, 0·112 grm.; in a control experiment, 0·356 grm. From a rabbit's liver, after ligature (for 17—29 hours), 0·095, 0·053, 0·115, 0·123, 0·088; thus showing a considerable diminution. The urine of all these animals contained blood-pigment, albumen, bile-pigments; but no sugar, as v. Wittich pointed out. In another series of experiments the rabbits were first allowed to starve for six days, the bile-duct was ligatured, and sugar given, to see whether, under these circumstances, glycogen would be formed. The amounts of glycogen obtained were 0·069, 0·039, 0·079 0·115, 0·066 grm. Even in well-nourished animals, without being previously starved, if the bile-duct was tied and sugar given, the amount of liver-glycogen was small—0·135—0·076 grm.

"On the Oxydation of Cholic Acid with Acid Chromate of Potash and Sulphuric Acid." H. Tappeiner, *Zeitschr. f. Biolog.* xii. 60, and *Centralblatt*, No. 42.——"On Bilifuscin." A. Simonof, *Sitzungsb.*

d. Wiener Acad. LXXIII. 3. Abth. 181.——"On Human Bile." N. Socoloff, *Pflüger's Arch.* XII. 54.——"On the appearance of Bile Salts in the Blood and Urine in certain forms of Poisoning." V. Feltz and E. Ritter (*Jour. de l'Anat.* 1876, 91, and *Centralblatt* No. 39) found these salts in the urine in poisoning with arsenic, arsenate of soda, tartar emetic, when given in such doses as not to cause the dogs to die for several days.

GENITO-URINARY SYSTEM.

ON THE EFFECT OF IRRITATION OF THE SKIN UPON THE SECRETION OF THE KIDNEYS.—Wolkenstein describes (*Centralblatt*, No. 31, 1876) the result of experiments made by him on the effects of the application of irritants to the skin of rabbits. He arrived at the following result. The action of different irritants is not constant. Slight irritation (by tincture of iodine, mercurial ointment, and solutions of tartar emetic) causes only a slight albuminuria, disappearing when the cause ceases to act. No changes in the kidneys are to be found in this case. When stronger means are applied (strong acids and caustics, moxas, &c.) the animals die in convulsions (apparently uræmic). The urine contains albumen (often in considerable quantity), epithelial cells from the uriniferous canals, and sometimes cylinders. The kidneys in these cases were enlarged, and their capsule distended and easily removable. The parenchyma of these organs was of a dirty reddish colour. The uriniferous canals were filled by finely granular epithelial cells in which no nuclei could be detected; the glomeruli were observed, and, even after treatment with solution of nitrate of silver, the outline of their epithelium could not be recognized.

In all the experiments—more than fifty in number—the following phenomena were observed. The temperature rapidly rose, and remained stationary as long as albumen was found in the urine. The pulse and respiration were quickened, and the animals became emaciated. When cantharidised collodion was used, the urine contained blood. The quantity of urine became less. Appetite and thirst were lost. There was increased excretion of urea and less of chlorides. The weight of the body decreased. There was noticed inflammatory reaction of the skin, with infiltration of the subcutaneous areolar tissue, etc.

The author explains the effect of the irritants in the following manner. The transudation of serum-albumen from the vessels into the uriniferous tubes depends either upon an increase of the blood-pressure, or upon changes in the walls of the vessels. Sometimes it is caused by a combination of both. When cantharides is absorbed by the skin it enters the circulation, and in being eliminated it produces albuminuria, in consequence of its action upon the vessels. Iodine acts in the same manner. Acids likewise probably penetrate the skin and produce diseases of the kidneys and vessels. Mercurial ointment also becomes absorbed and circulates as albuminates in the blood, and probably produced albuminuria in the urine, though this was not discovered, probably because it remains there for a longer

period, and was probably not yet eliminated when the search was made. No doubt the other irritants must cause albuminuria, for the reason that their application was followed by fever, constantly bringing forth a morbid state of the parenchyma of the organs and vessels. Lastly, albuminuria may also be caused by a disintegration of red blood-corpuscles.

Being under the impression that the nerves of the skin exclusively become irritated by an application of the electric brush, the author performed some new experiments, applying the irritation twice daily from six to ten minutes. This was followed: (1) by an increase of temperature and a greater frequency of the pulse and respiration; (2) by an increase in quantity of urine and urea, and by a decrease of the chlorides; (3) by slight albuminuria, which disappeared after from three to six hours. When the irritation was continued seven or eight days, there was much albuminuria, which lasted six hours, even when the irritant was not applied.—*Lond. Med. Rec.* Feb. 1877.

"On Mechanical, Chemical and Electrical Irritation of the Skin, and their effects on the Animal Organism." Dr Feinberg in *Centralblatt*, No. 39, 1876.

Urine.

"On the Fermentation of Urine." (C. Bastian *Comptes rendus*, LXXXIII., No. 8, and *Centralblatt*, No. 1, 1877).——"On the Origin of Phosphate of Lime excreted by the Urine." Pacquelin and Jolly, *France Méd.*, Nos. 80 and 81, regard the phosphate of lime found in the urine as, for the most part, formed during the secretion of the urine, by the action of phosphatic salts on the potash salts. Therapeutically phosphate of lime is of no use, for it is not absorbed.——"On the Hippuric Acid in the Bodies of Herbivora." H. Weiske (Kellner and R. Wienand), *Zeitsch. f. Biolog.* XII. p. 241, and *Centralblatt*, No. 6, 1877.——"On the Ferment of Urea." Musculus, *Comptes rendus*, LXXXII. p. 333, found that alcohol precipitated a substance from the urine of a patient suffering from bladder cataract, which, when washed with alcohol and dried, contained no organized elements, and was able to convert urea into carbonate of ammonia.

ON A NEW METHOD OF ESTIMATING THE AMOUNT OF ALBUMEN IN URINE.—J. Stolnikow, *Centralblatt*, No. 45.——"On Inosite." Kulz, *Marb. Sitzungsb.* 1876, No. 4.——"On the Origin of Indican in the Urine of Carnivora."——"On the Formation of Indol." E. Salkowski, *Ber. d. deutsch. chem. Ges.* IX. 138 and 408. All in *Centralblatt*, No. 45.——"On a phenol-forming substance in the urine." *Centralblatt*, No. 47, 1876.——"Is Grape Sugar a Normal Constituent of Human Urine?" E. Kulz (*Pflüger's Arch.* XIII. 269) got a negative result from 100 litres of urine obtained from two healthy men.——"On the Formation of Allantoin from Uric Acid in the Organism." E. Salkowski, *Ber. d. deutsch. Chem. Ges.* IX. 719, and *Centralblatt*, No. 48, 1876.——"On Conjugate Sulphates in Human Urine." R. v. d. Velden, *Centralblatt*, No. 49.——"On the Excre-

tion of potash-salts." A. Dehn, *Diss.* Rostock, 1876, and *Centralblatt*, No. 50.——"On the Non-existence of Mucus in the Urine." According to Méhu (*Bull. gén. de thér.* 1876, XCI. 161) this does not exist in urine. The cloud which forms when urine stands he regards as consisting of epithelial cells from the bladder and detritus of epithelium; and in the female in addition epithelium from the vagina and pus-cells.——"On Conjugate Sulphuric Acids in the Organism." E. Baumann, *Pflüger's Arch.* XIII. 285, and *Centralblatt*, No. 53.——"On Urobilin in Urine." J. Esoff, *Pflüger's Arch.* XII. 50.

ON THE EXCRETION OF OXALIC ACID BY THE URINE.—P. Fürbringer (*Deutsch. Arch. f. klin. Med.* XVIII. p. 143, and *Centralblatt*, No. 5, 1877) estimated the Oxalic acid by Neubauer's method, but finds that as the mean it gives results under the actual amount by 25 per cent. He finds that oxalic acid is a normal and constant constituent of the urine. Its amount does not seem to exceed 20 mgrms. per day. The amount of oxalate of lime precipitated as sediment on standing by no means necessarily corresponds to the entire amount of $\bar{O}$. acid in the urine. Urines occur which upon standing do not give any precipitate of oxalate of lime, but which are richer in oxalic acid than urines which give such a precipitate. The chief solvent for oxalate of lime is acid phosphate of soda. The less the acidity of the urine the greater the precipitate of its oxalate. The internal administration of bicarbonate of soda does not increase, but rather diminishes the excretion of $\bar{O}$. Even aq. calcis, taken in moderate amount (90—360 grms. daily), does not increase it. The administration of uric acid salts does not necessarily increase it. There is no constant dependence between the occurrence of a large quantity of oxalic acid in the urine and interruption of the normal processes of oxydation.

Tissue Metamorphosis.

"On the Influence of Respiration on the Tissue Metamorphosis." A. E. Pflüger, *Pflüger's Arch.* XIV. 1. Abstract in *Centralblatt*, No. 5. ——"On the Effect of Diminished Supply of O. on the Decomposition of Albumen within the Organism." A. Fränkel, *Virchow's Arch.* LXVIII. p. 1, and *Centralblatt*, No. 5.

ON THE ACTION OF SALICYLIC ACID AND ITS SODA-SALT ON THE METAMORPHOSIS OF THE TISSUES.—S. Wolfsohn (*Diss.* Königsberg, 1876), working under Jaffé, experimented on dogs. He concludes that salicylic acid increases the decomposition of the tissues in a manner similar to that which Salkowski showed for benzoic acid. This action cannot be ascribed to the increased diuresis. In several experiments a diminution of the temperature was observed after the introduction of the acid.

Skin.

THE PHYSIOLOGY OF THE SKIN TREATED EXPERIMENTALLY AND CRITICALLY.—A. Röhrig, Berlin, 8vo. pp. 217. Abstract in *Central-*

blatt, No. 45, 1876.——"On the Blood-pressure in the Capillaries of the Human Skin." N. v. Kries, *Ludwig's Arbeiten*, 1857.

Milk.

"On the Physiology of the Secretion of Milk." A. Röhrig, *Virch. Arch.* LXVII. p. 119, and *Centralblatt*, No. 41, 1876.——"On Lacto-protein." O. Hammarsten, *Nord. Med. Arkiv*, VIII. Hft. 2.——"On the Quantitative Estimation of Albumen in Milk." J. Puls, *Pflüger's Arch.* XIII. 176, and *Centralblatt*, No. 50.

Muscular and Ciliary Motion.

ON THE THEORY OF DOUBLE MUSCULAR ACTION.—Chirone (*Revista clinica di Bologna*, Oct. and Nov. 1876) discusses the question whether the cardiac diastole and dilatation of the arteries are due to muscular action. He holds that, while none of the existing theories explain the facts connected with these phenomena, the rhythmical contraction in the arteries is not the cause but the effect of an increased afflux of blood.

He further holds that smooth muscular fibre is endowed with double action, and that its fibres are composed of primary elements of an ovoid form, arranged in the muscle at rest in a parallel direction somewhat obliquely. When rotated vertically these elements cause contraction, with shortening and enlargement of the muscle: when in a more oblique direction, they cause elongation and extension.

With this double muscular action are connected two series of nerves—contractile and extensile, examples of which are seen in the heart, vessels, intestine, and uterus. Certain agents, such as the poison of the toad, atropine, and cold, promote contractility, while others, such as quinine, chloral, &c., favour dilatation.

With the aid of muscular extension the author explains many facts; strong stimulation of the vagus-nerve prolongs the diastole; stimulation of the central end of a divided nerve, such as the sciatic, produces dilatation of the vessels, &c. These acts of dilatation cannot be completely explained by any other theory. [*Lond. Med. Rec.*, Feb. 1877.]

"On the Height of the Contractions in Muscles stimulated with over-maximal stimuli," and "The Height of the Contraction of Muscle as a function of the Weight." E. Tiegel, *Ludwig's Arbeiten*, 1875, and *Pflüger's Arch.* XII. 133.——"On the relation between Weight and Height." L. Hermann, *Pflüger's Arch.* XIII. 369, all in *Centralblatt*, No. 38.——"On the Blood-current in Muscle." W. H. Gaskell, *Centralblatt*, No. 32, and *Proceedings of Royal Society*, 1877. In extenso in this Journal.——"Warming of Muscle during Extension." J. Steiner, *Pflüger's Arch.* XI. 196, and *Centralblatt*, No. 25.——"Contractility and Double Refraction." W. Englemann, *ibid.*

ON THE TRANSMISSION OF CONTRACTION AND NEGATIVE VARIATION IN THE MAMMALIAN MUSCLE.—J. Bernstein and J. Steiner (*Reichert*

and du Bois' Arch., 1875, 526, and *Centralblatt*, No. 53). The identity in the rapidity of contraction and negative variation in the frog's muscle led to similar experiments on the mammalian muscles. The experiments on the rapidity of muscular contraction were made on the sterno-mastoid of a curarised dog, the muscle being divided at its sternal end and arranged on a gutta-percha trough provided with electrodes for stimulation. Several modifications of apparatus were employed, including Du Bois Reymond's Spring-Myographin, Helmholtz's Myograph, and Marey's Polygraph. All these methods gave the same result, viz. that the rapidity of transmission varied between 3 and 4 metres per sec., *i.e.* 3·5 as the mean,—but still for various reasons, it must be reckoned at 4—5 metres. The stage of latent stimulation was found to be in one case 0·017, and in another 0·028 sec., thus not essentially differing from that in the frog's muscle. On the contrary, the duration of the wave of contraction (0·27—0·49″) was much greater than in the frog, but in the intact rabbit's sterno-mastoid the value was nearly that in the case of the frog, so that probably the high value in the case of the dog's muscles depends upon imperfect nutrition of the muscle.

Very considerable difficulties presented themselves in estimating the rapidity of transmission of the negative variation, but two successful experiments on rabbits' muscles gave values of 2·5 metres per sec. On stimulating the nerve the gastrocnemius yields qualitatively and quantitatively the same phenomena as in the case of the frog.

THE FORCE OF CILIARY MOTION.—Bowditch (*Boston Med. and Surg. Journal*, 1876) repeated J. Wymann's experiment, who found that the amount of work that could be done by the action of cilia was very considerable. He found, for instance, that a weight of 1·3 grms. placed on a piece of mucous membrane measuring 12 mm. square excised from the palate of the frog, moved forward 15 mm. in a minute, and that even with a weight of 48 grms. the whole mucous membrane still moved forward, though of course very slowly.

Bowditch finds that the greatest amount of work is obtained with the smallest weights, and with increasing weights the rapidity of motion decreases, but not proportional to the increase in weight, but in an increasing ratio. The maximum amount of work for every cm. square of surface Bowditch reckons to be 6·805 grm.—mm. per minute.

Bone.

ON THE EFFECT OF LACTIC ACID ON THE BONES.—Can the introduction of lactic acid into the intestines of an animal remove inorganic constituents from the bones? This question was answered in the affirmative a short time ago by Heitzmann, who asserted that, on feeding graminivorous animals with lactic acid, osteomalacia could be produced; and that in flesh-eaters, first rachitis, and then osteomalacia occurred. E. Heiss tested the above assertions on a dog. The experiments lasted over a year, and the animal got in all 2,286

grammes of lactic acid. On examining the bones they were found to be normal throughout. Lactic acid was not present, or if so, only in traces, in the urine. The carefully conducted analysis showed that the lactic acid had removed no lime from the body. [*Lond. Med. Rec.* Jan., 1877.]

Temperature.

"On the origin of the Bodily Temperature and on Fever." S. Samuel, Leipzig, 1876, 8vo. pp. 138, and *Centralblatt*, No. 47, 1876.——"On the Cooling of the Body from the Rectum." D. C. Rutenberg, *Deutsche med. Wochensch.* 1876, No. 19, *Centralblatt*, No. 45.——"On the Effect of Cutaneous Stimulation on the Bodily Temperature." L. Jacobson, *Virch. Arch.* LXVII. 166, and *Centralblatt*, No. 48.——"The Analogies to Dulong-Petit's Law in Animals." A. Adamkiewicz, *Reichert u. du Bois-Reymond's Arch.*, 1875, 78.——"The Thermal Conductivity of Muscle." *Ibid.* 233.——"The Mechanical Principles of Homö-othermie in the Higher Animals, etc." *Ibid.* 1876, 248. All in *Centralblatt*, No. 50, 1876.——"On Cooling of Warm-blooded Animals." A. Horvath, *Pflüger's Arch.* XII. 278.

TEMPERATURE OF PERIPHERAL PARTS.—M. Adae (*Diss.* Tubingen, 1876), working under Liebermeister, found that on *interrupting the arterial circulation* in the arm by compressing the brachial artery, the temperature of the palm of the hand of the same side sank 2° C. and the same effect was produced by the fillet used in venesection causing *venous congestion.* *Bodily exertion* caused a decrease of the temperature of 1·75° C. in the closed palm, while that of the corresponding axilla rose 0·1 to 0·5°. The temperature of the palm only rose after the exertion had been continued for a long time. After the taking of wine, the temperature of the palm generally sank, while in the axilla it varied. The same was the case when beer was taken.

Miscellanea.

"On the Physiological action of Nitro-pentans, -aethans, and -methans." W. Filehne, *Centralblatt*, No. 49, 1876.——"On the action of Musk." W. Filehne, *Sitzungsb. d. Erlang. Physic. Med. Ges.*, 1876, and *Centralblatt*, No. 49.——"On the alkaloids of Fungi." M. Schiff, *L' Imparziale*, 1876, *Centralblatt*, No. 50, and *London Med. Rec.*, 1876.——"On the action of Butyl-chloral on Rabbits." H. Windelschmidt, *Centralblatt*, No. 50.——"On the action of Anemonin on the Animal organism." Curci, *Lo Sperimentale*, 1876, XXXVIII., No. 7, and *Centralblatt*, No. 51.

A NEW FORM OF INDUCTION APPARATUS.—P. Bowditch (*Proceed. of American Acad. of Arts and Sciences*, 1876, p. 281) in a short note describes a modification of the du Bois Induction Machine. In this apparatus, if we wish to graduate the intensity of the current by the approximation of the secondary to the primary coil one meets

with the difficulty that the intensity increases incomparably rapidly, viz. inversely as the square of the distance. This difficulty Bowditch tries to lessen by placing the secondary coil at right angles to the primary and causing the secondary coil to rotate round a vertical axis. The intensity is then found to be proportional to the cosine of the angle of rotation, which is indicated by a divided circle placed on the apparatus which gives the intensity of the current.

THE PHYSIOLOGICAL ACTION OF QUININE.—According to N. Jerusalimsky (Berlin: Hirschwald, 1875, and abstract in *Centralblatt für die Medicinischen Wissenschaften*, No. 26, 1876), quinine given in small and medium doses (1 to 5 grains) always causes in dogs (rabbits and frogs are less suited for these experiments) an increase in the freqnency of the pulse, it may be even doubled and more. Variations occur, but it never falls under the normal. The pulse sinks rapidly just before death. The blood-pressure, on the contrary, has in general the tendency to fall, only after each injection there is a short period where, with variations, it rises somewhat; then it gradually falls under the normal, though not far under, as long as no large doses are given. Large doses (20 to 25 grains) cause the pressure to sink rapidly and generally at once, but the pulse frequency, generally after a short acceleration. The acceleration of the pulse, as is shown by special experiments (section of the vagi, of the spinal cord at different heights), is the result of a depression or paralysis of the regulating and excitation of the excito-motor nervous system.

The condition of the blood-pressure—with medium doses a short increase lasting between twenty and sixty minutes, then sinking, notwithstanding increased pulse-frequency—is explained by the author through a complicated nerve-action. The increase is caused by paralysis of the regulating and stimulation of the vaso-motor apparatus. That the vaso-motor centre in the medulla participates is supported by this, that after its destruction the increase is only feebly expressed. The effect of quinine on the vessels was ascertained by direct observations on the frog, and specially by the experiments on the spleen to be presently cited. After the excitation of the vaso-motor centre paralysis follows very rapidly, which affects the peripheral vessels, the excito-motor cardiac ganglia and the cardiac muscles. After large doses the heart itself does not reply to direct stimulation. The conditions here mentioned are those which follow medium doses; after small doses the tonic action, after large the paralytic is more pronounced. In man, the author, after a moderate dose (10 grains), observed acceleration of the pulse, and increased heart-beat, which in one case increased to palpitation. The cause of the difference in the results between this and other authors, the author seeks to ascribe to difference in the animal employed.

The respiration is always increased by small doses, slowed by large doses, and also rendered irregular with rapid following asphyxia. This action arises from the effect on the respiratory centre. The hyperæmia and even the hæmoptysis observed by some authors after

large doses of quinine are probably due to paralysis of the vaso-motor centre by the quinine.

The action on the temperature was not constant throughout. In most experiments it sank (at most 1·5° Cent. 2·7° Fahr.); in other cases it rose, and this after large doses, and in other cases it varied little from the normal. The author explains these results by the action of quinine on supposed nerve-centres. After section of the spinal cord, (1) between the sixth cervical and first dorsal vertebra there was pronounced increase of temperature (3° to 4° Cent. 5·4° to 7·2° Fahr.); (2) in the region of the second dorsal vertebra the reverse, and (3) under the second to the sixth dorsal vertebra, only slight modifications from the normal. The author assumes the existence of a heat-exciting centre, opposite the second dorsal vertebra, and a heat-regulating centre, between the sixth cervical and first dorsal vertebra, which influence the exchange of material through trophic nerves. The author explains the modification in temperature, by the relation of quinine to these two centres. The increase after large doses would therefore be produced by paralysis of the regulating centre.

The rapidity of the blood-current (investigated by Ludwig and Dogiels' Stromuhr) is much slowed by quinine, in the proportion of 1 : 2 and more. This phenomenon is specially to be ascribed to the paralysis of the vaso-motor centre, for after its destruction quinine can only produce a very slight retardation.

With regard to the effect of quinine on the colourless blood-corpuscles, the author confirms the statements of Binz and his scholars. He also observed cessation of the amœboid movements; emigration and diminution in the number of these bodies. Further, he observed that the corpuscles which had emigrated had for the most part a single nucleus, whilst previously the greater number were multinucleated. Like Manassein, he observed that the red corpuscles became larger under the influence of quinine.

Confirming Mosler, he observed also the diminution in the size of the spleen; the organ becoming at the same time tougher, granulated on the surface, and of a brighter colour. After section of the splenic nerves (splenic plexus, or semilunar ganglion or splanchnic) or of the spinal cord, which produced of course a considerable swelling of the spleen due to paralysis of the vaso-motor nerves, the effect of quinine still occurred, though to a much less extent. It therefore depends primarily on the effect of the alkaloid on the peripheral nervous and muscular elements of the spleen, and secondarily on the splanchnic and central nervous system.

The Physiological Action of Nitrite of Amyl.—S. Mayer and J. Friedrich (*Arch. für exper. Path.*, Band v. p. 55, and *Centralblatt für die Medicin. Wissenschaften*, No. 38), in order to avoid the disturbing effects produced by inhaling this drug through the nose, invariably administered it through a tracheal cannula, and according to the duration of inhalation of the vapour, they distinguished a weak (4·60 sec.) or a strong dose (over a minute). These observers,

like Filehne, always observed a considerable increase in the frequency of the pulse produced by the amyl nitrite. In the explanation of this phenomenon they also agree with Filehne, in ascribing it to a diminution of the tonus of the vagus centre, and adduce several new facts in support thereof. In dogs, which have received amyl nitrite, the difference in the number of beats during inspiration and expiration disappears; further, if in curarised animals, when by stopping the artificial respiration, the number of heart-beats has been reduced, in consequence of stimulation of the vagus centre by the dyspnœic blood, a small quantity of amyl nitrite is injected into the jugular vein, the frequency of the heart-beats increases just as if the vagi were divided. Large doses of amyl nitrite paralyse the heart itself.

Regarding the fall in blood-pressure produced by amyl nitrite, the authors have succeeded in affording a new proof of the view of Lauder Brunton, that this drug acts directly on the walls of the vessels. After the method of Kussmaul and Tenner, by cutting off the supply of blood to the brain and medulla oblongata, they rendered these organs inactive, so that all phenomena depending upon these centres ceased. If amyl nitrite was now inspired, the blood-pressure fell considerably.

After moderate doses the respiration became more frequent and deeper; after strong doses flat and very slow. In this case, it is due to a direct action on the respiratory centre. That the change in the blood-circulation does not produce the dyspnœic respiration, is proved by an experiment with diminution of the blood-pressure by stimulating the nervi depressores. In this case acceleration of the respiration only occurs here and there, although the diminution of the blood-pressure is greater than that produced by the amyl nitrite.

The spasms produced by this drug are not caused by the changes in the circulation, but are due to a direct stimulation of the brain. The spinal cord does not appear to be influenced thereby.

After inspiring the vapour for a considerable time, the animals pass into a condition where the blood-pressure falls very low, the heart-beats and the respiratory movements slow, but regular, and the peripheral nerves and the muscles remain excitable. As this stage lasts for a long time (one hour), it may be probably of value for some experiments.

THE LOCAL ACTION OF THE SO-CALLED ASTRINGENTS ON THE BLOOD-VESSELS.—H. Rosenstirn (*Würzb. Phys. Med. Verhandlungen*, IX. p. 32, and *Centralblatt für die Medicin. Wissenschaften*, No. 35) tested solutions of nitrate of silver, acetate of lead, tannic, gallic, and pyrogallic acids, sesquichloride of iron and alum, by placing them upon the mesentery of a curarised frog, and estimating the size of the lumen of the affected vessel by means of the microscope. Nitrate of silver acted most powerfully on the vessels; it was employed in solution from 1 to 10 per cent. The observation was often interfered with by the turbidity produced in the tissues. The contraction extended to about half the lumen of both arteries and veins, and in a much less degree in the capillaries. The reaction

occurred within a few seconds. Stagnation generally took place in the vessels, permanent in the capillaries, and temporary in the arteries and veins. Tannic acid had exactly the opposite effect. Under its influence the arteries dilate, even the veins and capillaries to the extent of one-half of their lumen, and appear to be over-filled with blood-corpuscles. The dilated vessels become narrowed at once by the action of nitrate of silver. Gallic and pyrogallic acids have an action similar to tannic acid. Acetate of lead acts more feebly than nitrate of silver. It narrows the arteries and veins, but no effect was observed on the capillaries. Sometimes also standstill of the circulation occurs. A 10 per cent. solution of sesquichloride of iron had no effect; in a 50 per cent. solution it narrowed the vessels less than acetate of lead. This narrowing is limited to the arteries and veins, while the capillaries dilate. Coagulation and discoloration of the blood within the vessels often occur. The results of the alum solution were variable.

In order to exclude a reflex action, the spinal cord was destroyed and the heart ligatured.

The author therefore ascribes an astringent effect, *i.e.* contraction of the vessels, only to nitrate of silver and acetate of lead; whilst this action is doubtful for alum and solution of sesquichloride of iron, and is certainly not the case with the group to which tannic acid belongs.

THE PHYSIOLOGICAL ACTIONS OF COLCHICIN.—J. Rossbach (*Pflüger's Archiv*, Band XII.) remarks that the most striking phenomenon produced by this drug is the complete loss of sensibility by paralysis of the peripheral and the central nerve terminations. The reflex excitability is extinguished. The motor nerves and the muscles preserve their excitability till death. In many animals the paralysis is preceded by a stage of excitation, which in frogs may proceed to a spasmodic attack. The circulation of the blood is only slightly affected by the poison. The heart continues to beat even after the appearance of the paralysis of the central nervous system. The blood-pressure remains long unchanged, and sinks only at death, and the paralysis of the inhibitory cardiac nerves also occurs late. The respirations gradually become less frequent, until complete standstill occurs, so that one must conclude that the respiratory centre is paralysed. In warm-blooded animals, and especially in cats poisoned with this drug, the whole gastric and intestinal mucous membrane was swollen and strongly injected, and bloody mucus was found in the intestine. As a consequence of this, during life there was diarrhœa, vomiting, and colic-like pain. The cause of the strong injection of the vessels was not determined. The fibres of the splanchnic and abdominal vagus were not paralysed. The kidneys were also strongly hyperæmic and their secretion diminished.

The action of colchicin occurs very slowly, and death only takes place after several hours. It is remarkable, as Schroff had already indicated, that the amount of the dose has no important influence either on the intensity or on the rapidity of the poisoning. A few

centigrammes, in cats several milligrammes, suffice to produce death, which occurs through stoppage of the respiration, the heart still continuing to beat. In this stage tonic or clonic spasms sometimes occurred in rabbits and cats. These the author regarded as the spasms of asphyxia. Doses smaller than are lethal have no effect.

The author, therefore, does not regard colchicin as a therapeutic agent of much value. It may be used as a local anæsthetic, and Gerhardt uses it as such, for application to the mucous membrane of the pharynx and larynx.

On the Local Action of Sulphate of Atropin.—A. Zeller (*Virch. Arch.* LXVII. 384) finds that a half per cent. sulphate of atropin in NaCl solution abolishes the movements of the colourless corpuscles after a short time.

On the Influence of Etherisation on Vital Phenomena. —(*Progrès Médical*, November 4, 1876.) Bernard had shown that anæsthetics suppress, during their action, some vital phenomena, movements of the sensitive plant, germination of cresses, fermentation of beer-yeast, &c. His recent experiments have been made on the lower animals—small eels. It is known that these animals when dry lose all movement, and remain inert, but it is sufficient to place them in water to see them resume their movement. If we plunge them in pure chloroformed water the movements disappear, and immersion in water will not bring them back; the animals are dead. But if we plunge them into a chloroformed solution diluted with its weight of water the movements cease, the animals fall inert. On withdrawing them from this liquid to place them in water, however, the movements are renewed; in this the anæsthetic action has not been strong enough to kill the animals. Etherised water acts in a similar manner, but with less intensity than chloroform.

How do the anæsthetics act? Their action is exerted on all the elements as well as on the nervous system, which is the first affected. The exact nature of the phenomena must still be sought; nevertheless it seems probable that it is the protoplasm which is modified by the anæsthetic agent. It has been remarked that the muscles during etherisation become opaque, and recover their transparency on its cessation.

M. Berthelot has suggested that anæsthesia in vegetables and animals may be due to a chemical modification of a substance, analogous to the proximate principles of the cerebral substance, which has been found existing in the sensitive plant and in the seeds of vegetables.

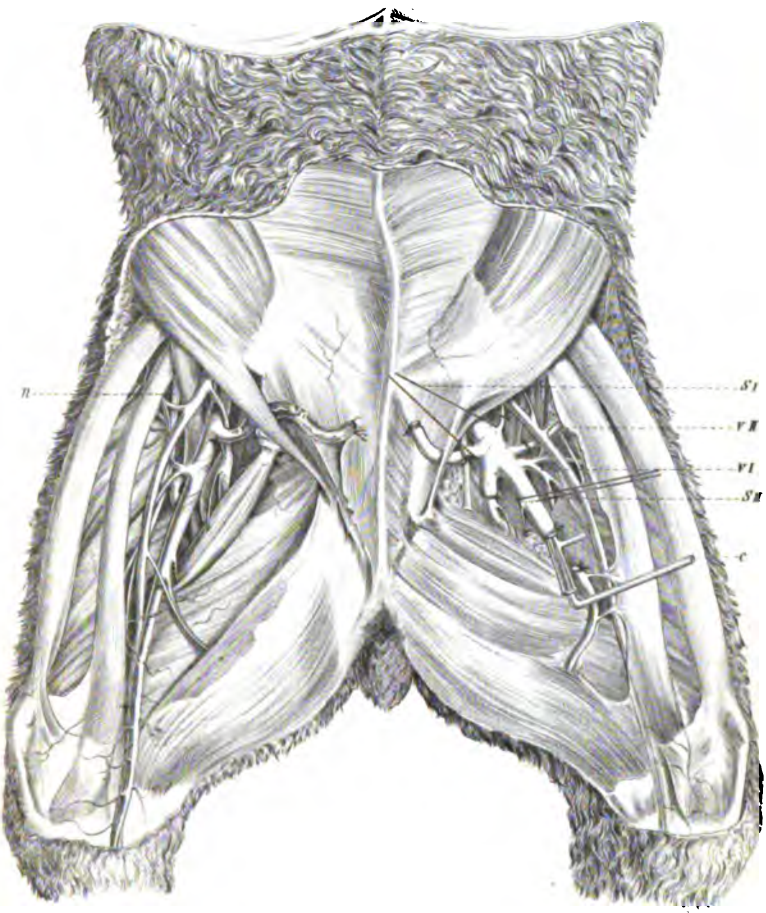
Das Princip des Wachsthums.—F. Boll, Berlin 1876; pp. 82. 1 plate.

Text Books.

"Text Book of Physiology," by Michael Foster.

R. M. Gunn. del.

T. P. Collin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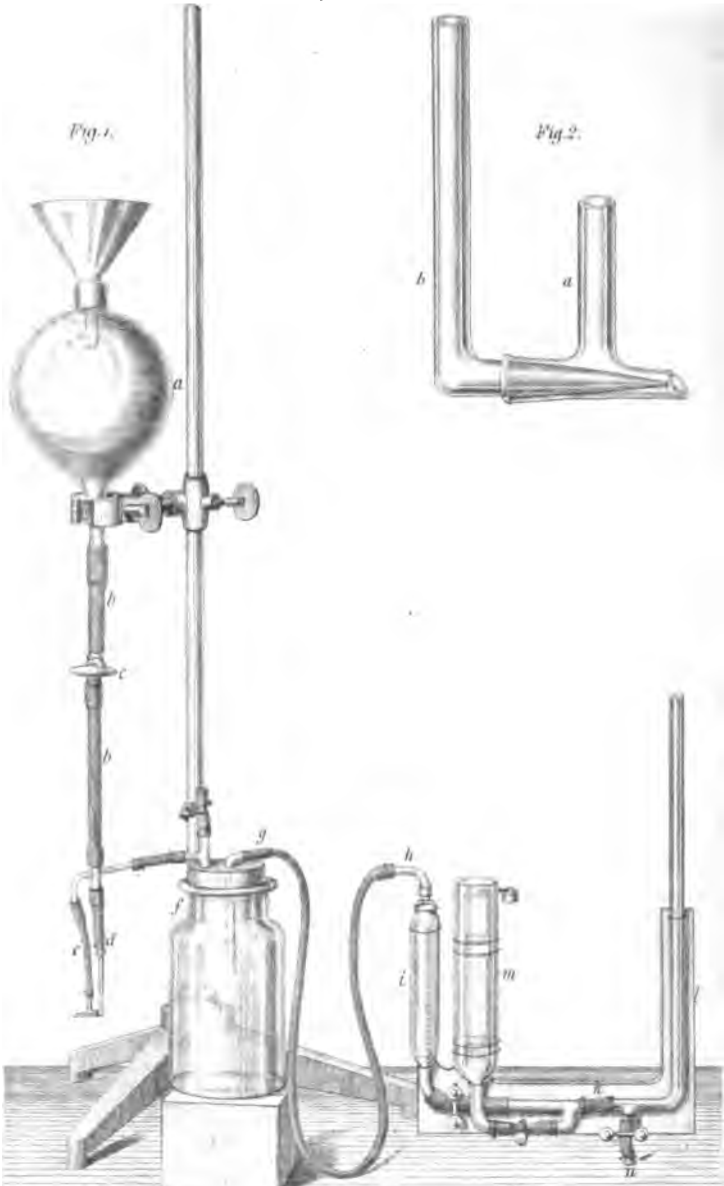
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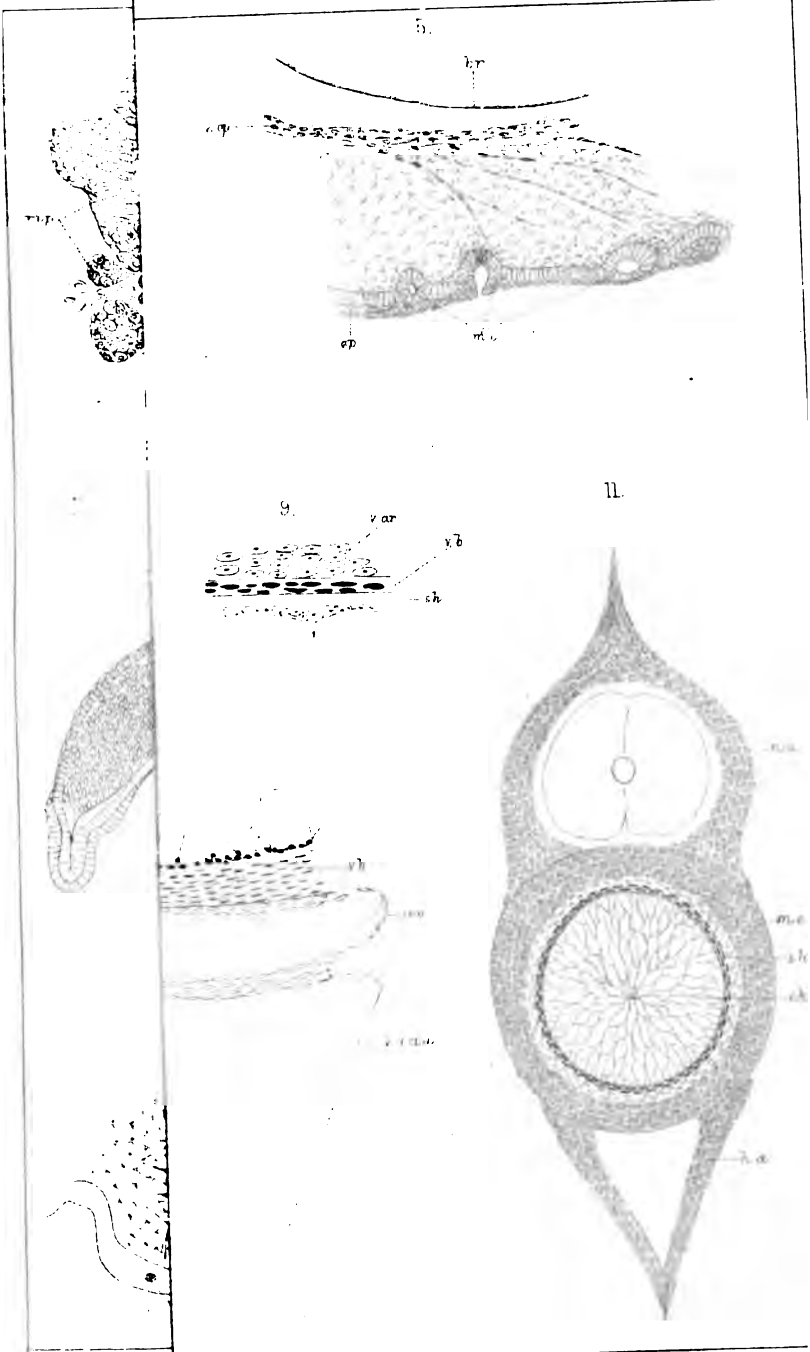

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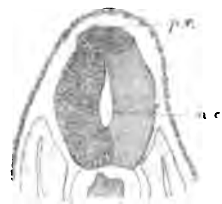

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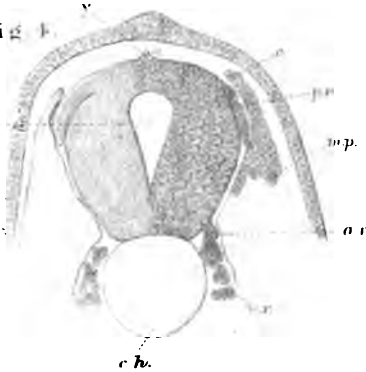

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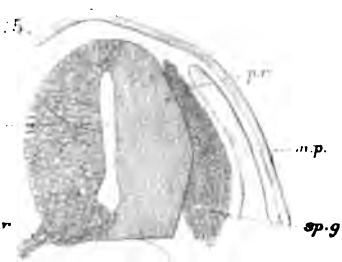

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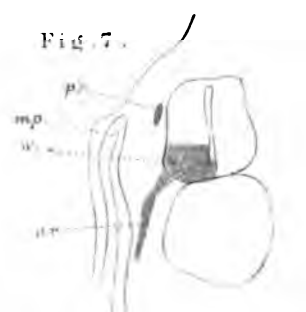

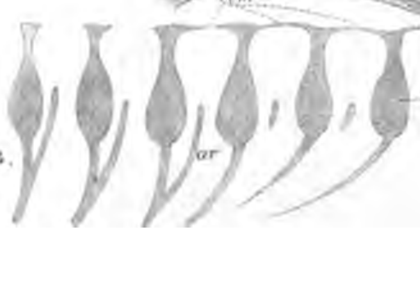

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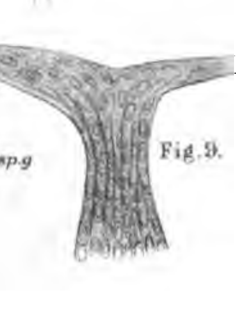

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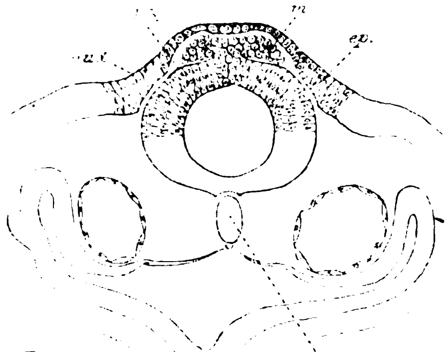

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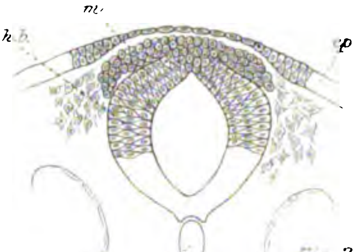

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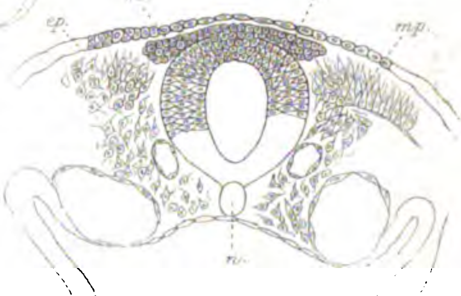

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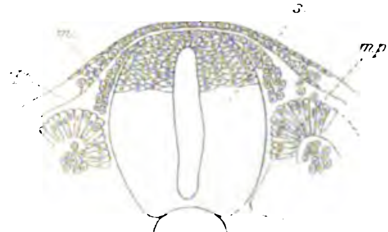

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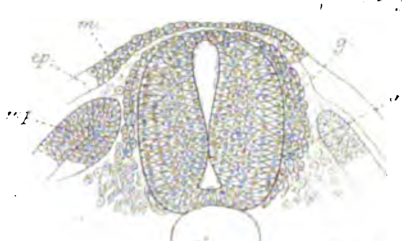

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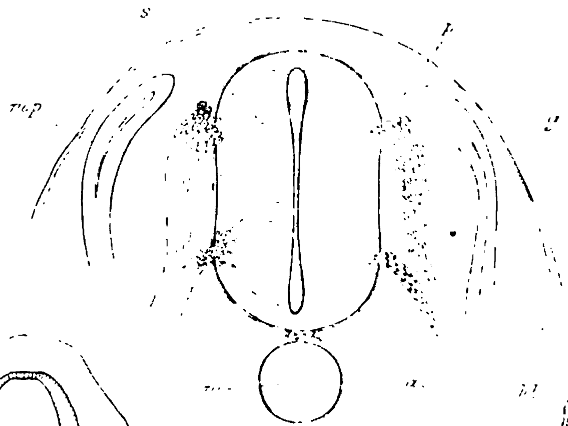

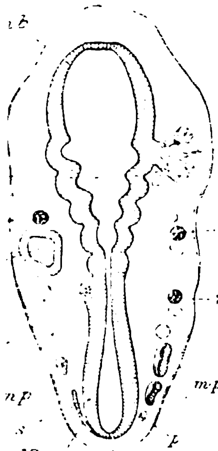

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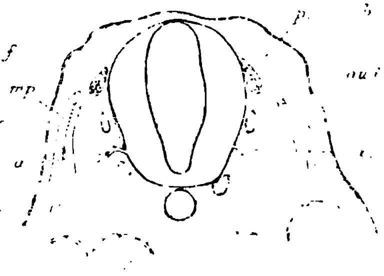

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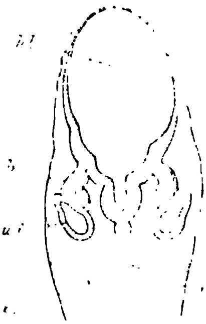

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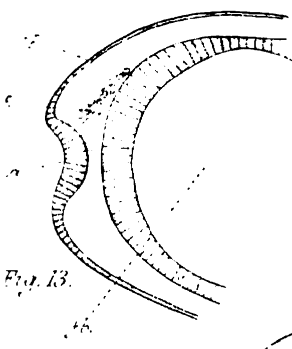

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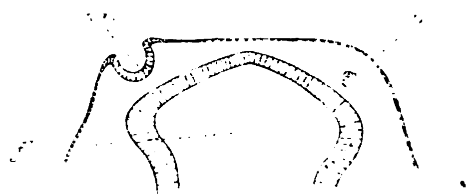

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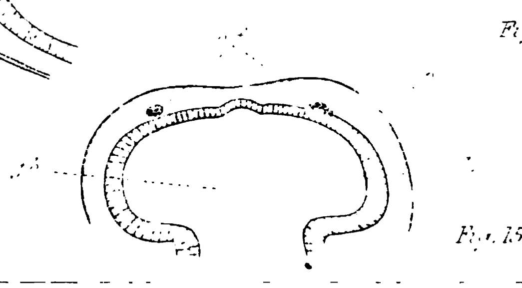


Fig. 15

Journal of Anatomy and Physiology.

ON THE FORMATION OF FAT IN THE ANIMAL BODY[1]. By J. B. LAWES, M.D., and J. H. GILBERT, M.D.

PLATE XXII.

FORMERLY it was supposed that the fat of the Herbivora was derived exclusively from ready-formed fat in their vegetable food. Liebig showed that this could not be the case; and he attributed much of the fat of the animal body to the carbohydrates of the food. His views on the point were at first called in question by Dumas, Boussingault, and others, but afterwards accepted. Our own very numerous feeding experiments, commencing about 30 years ago, together with a careful consideration of the experience of practical feeding, afforded strong confirmation of Liebig's conclusions; and more especially in 1852[2], and subsequently, we pointed out the bearing of the results on the question.

At a meeting of the Congress of Agricultural Chemists held in Munich, in 1865, Professor Voit combatted this view. From the results of experiments with dogs, made in Pettenkofer's respiration-apparatus, he maintained that fat must have been produced from the transformation of nitrogenous substance; and further, that this was probably the chief, if not the only, source of the fat, even of Herbivora. In 1869 he elaborately argued the point, not only in reference to the results of his own experiments with dogs and with cows, but also to the records of those of various other experimenters, with various descriptions of animal; and he has subsequently made further contributions on the subject, conjointly with Professor Pettenkofer. If their results, obtained with a dog, and their conclusions

[1] The substance of this paper was given by one of us at the Naturforscher Versammlung (Section für Landwirthschaft- und Agricultur-Chemie) at Hamburg, in September, 1876.

[2] On the Composition of Foods in relation to Respiration and the Feeding of Animals. *Report of the British Association for the Advancement of Science, for* 1852.

drawn from them, were to be described in a few words, they might perhaps be so as follows:—When a dog was fed on starch or sugar, alone, or with albumin, or with fat and albumin, the carbon stored up was not more than that in the fat of the food *plus* that which could be derived from the albumin broken up. There was, therefore, no proof that fat can be formed from the carbo-hydrates. Again, when a dog was fed with starch and a little fat, but no albumin, the carbon stored up was equal to that of the fat of the food *plus* that derived from the transformed nitrogenous substance of the body. More starch reduced the amount of carbon stored up; the carbo-hydrate having protected the albumin of the body from oxidation, and thus limited the formation of fat. They never found fat formed from starch or sugar. They maintain that the same must occur with the Herbivora; and that to establish the formation of fat from the carbo-hydrates, experiments must be brought forward in which the fat deposited is in excess of that supplied by the food *plus* that which could be derived from the transformed albumin.

This, many of our own experiments with pigs do clearly show; and in 1866 we published a short paper[1], in which we illustrated the bearing of some of them on the point. In his paper in 1869[2], Professor Voit quotes some of those results, and admits that in the experiments in which there was only a medium albuminous supply in the food, there was, as the figures stand, a considerable deficiency for the formation of the fat produced, and a greater deficiency still in the cases in which the relation of the nitrogenous to the non-nitrogenous constituents was such as experience has shown to be the most favourable for pig-fattening; and that, therefore, a considerable amount of fat would, in these instances, appear to have been derived from the carbo-hydrates. Still, Professor Voit says he cannot allow himself to consider a transformation of carbo-hydrates into fat to be proved thereby. He confesses that he has not been able to get a general view of the experiments out of the mass of figures recorded, and suggests several possible sources of error, his reference to some of which shows that he has in fact misunderstood them. At the same time, he proposed that new

[1] On the Sources of the Fat of the Animal Body. *Philosophical Magazine*, December, 1866.

[2] *Zeitschrift für Biologie.* Band v.

experiments with geese and with pigs should be made, in order to arrive at a final decision on the question; and in a very recent conversation with one of us, he expressed his willingness to undertake a conclusive experiment with pigs.

Weiske and Wildt[1] undertook an investigation to determine the point; which, from a theoretical point of view, was well conceived; but which did not succeed, owing to the oversight of the conditions indicated by experience as essential to the rapid fattening of the animal. They selected four pigs; two were slaughtered to determine the initial composition; one was fed on food so rich in nitrogen that it suffered in health, and the experiment had to be discontinued; the other was fed on food so poor that it fattened extremely slowly; and hence, at the conclusion, calculation showed that there was enough of the consumed nitrogenous matter available for fat-formation to cover the whole of the fat which had been produced.

Thus, it has been concluded from experiments with animals which are not preeminently fat-producers, that fat is probably never formed in the body from the carbo-hydrates; and some of the experiments with more suitable animals have been, to say the least, inconclusive. Further, it seems to be assumed, that no absolute proof on the point can be obtained without the aid of a respiration-apparatus. These views, moreover, have already been adopted, not only by some physiologists, but in some text-books treating of the application of chemistry to the feeding of the animals of the farm. Thus, Professor Emil Wolff, in his *Landwirthschaftliche Fütterungslehre*—although he admits that the amounts of increase produced in relation to constituents of food consumed, which it is established by common observation may be obtained with pigs, and still more those recorded in some direct experiments with those animals, are almost incomprehensible without assuming the direct concurrence of the carbo-hydrates in the formation of fat—nevertheless, seems to consider that evidence of the kind in question, and we suppose our own, therefore, is inconclusive. He says that exact experiments are still wanting; and he suggests that accurate respiration-experiments with pigs should be made, to settle definitively whether the carbo-hydrates, as well as albumin, can contribute directly to the formation of fat in the animal body.

[1] *Ib.* Band x.

Since the appearance of Professor Emil Wolff's work, and the publication of the negative results of Weiske and Wildt, we have carefully reviewed and recalculated many of the results of our feeding experiments, including those with oxen, with sheep, and with pigs; in order to satisfy ourselves whether any doubt could be entertained of the views we have previously advocated; and whether, therefore, it was at all incumbent upon us to institute new experiments on the point. The result of this examination, so far as the ruminant animals are concerned, has been to show that, owing to the comparatively small amount of increase obtained with them from a given amount of constituents consumed, the quantity of nitrogenous substance passed through the system for the production of a given amount of increase was, in most, if not in all cases, so large as, in the absence of proof to the contrary, to admit of the assumption that the whole of the fat formed had its source in transformed nitrogenous matter. At any rate, no absolute proof of the derivation of fat from the carbo-hydrates can be obtained from data of the kind in question relating to such animals. In deciding the point in regard to them, the evidence afforded by the analysis of the fæces and of the urine, and by the determination of the products of respiration, must also be brought into consideration. It was quite otherwise, however, in the case of our experiments with pigs; in many of which much more fat was produced than could possibly have been derived from transformed albumin of the food. We concluded, therefore, that we were in no way called upon to institute new experiments, and decided, instead, again to direct attention to the results quoted in the short paper on the subject published in 1866, as already referred to.

The figures given in Table I. of that paper show how much smaller is the proportion of alimentary organs and contents in a given live-weight of the pig than of either oxen or sheep; that, in proportion to a given live-weight, the pig consumes a very much larger quantity of dry substance of food within a given time (whilst his food contains a very much larger proportion of digestible, and therefore, very much less of necessary effete matter); that he gives several times as much increase in relation to a given live-weight within a given time; much more increase in relation to a given quantity of dry substance

of food; also a larger proportion of fat in that increase. Further, the most appropriate fattening food of the pig contains a larger proportion of readily digestible carbo-hydrates than that of the ruminant animals. All these conditions indicate the pig to be the most suitable animal for the determination of the point in question.

The results selected to illustrate the main point are given in Table II. of the same paper. They were all obtained more than 20, and some more than 25 years ago; and the rations were not arranged with a special view to the settlement of this question; but to determine the relations of the different constituents of food to various exigencies of the body, and the amount, and the proportion of different foods which were the most favourable for the feeding of the animals. Accordingly, the series included proportions varying from 2·0 to 6·6 parts of non-nitrogenous to 1 of nitrogenous substance in the food.

In experiment 1, two animals were selected, of the same litter, and as nearly as possible alike both in character and weight; the weight of the one being 100 lbs., and that of the other 103 lbs. One was slaughtered at once, and its contents of nitrogenous substance, fat, mineral matter, &c., accurately determined. The other was fed on a mixture consisting of bean-meal, lentil-meal, and bran, each one part, and barley-meal three parts, given *ad libitum*, but accurately weighed, for a period of ten weeks, when it had nearly doubled its weight. The food contained, however, a considerably higher proportion of nitrogenous to non-nitrogenous constituents than is recognised as the most favourable for the fattening of the pig. The animal was then slaughtered, and analysed, as the other had been. The composition of the food was also determined by analysis. The experiment afforded, therefore, reliable data for determining the amounts of fatty and nitrogenous substance consumed, the amount of nitrogenous substance stored up in the animal as such, and also the amount of fat stored up.

Eight other experiments were quoted, in each of which a different food-mixture was employed, and in each of which three animals were fed, in some cases for a period of eight, and in others of ten weeks. The average live-weight per head at the commencement was, in these eight experiments, respec-

tively, 143, 147, 144, 149, 95, 95, 94, and 97 lbs. Thus, in the first four cases, the average initial weight per head was notably more than that of the two animals of experiment 1; but in the last four experiments it was very nearly the same. In the calculations, the percentage composition of the animals in experiments 2—9 was assumed to be the same at the commencement as that of the unfattened animal in experiment 1, and the same at the conclusion as that of the fattened animal in experiment 1. It was quite obvious, during the progress of the experiments, that the animals having the higher proportions of nitrogen in their food, grew more, and fattened less, than the others; and careful observations, made after slaughtering, entirely confirmed this. The tendency to error in the calculations would be to indicate too low an amount of nitrogenous substance, and too high an amount of fat stored up in the cases with the higher proportions of nitrogenous substance in the food, and too high an amount of nitrogenous substance, and too low an amount of fat stored up with the lower proportions of nitrogenous substance consumed. The range of the probable error here supposed is, however, not such as at all to throw doubt on the validity of the main conclusions which are drawn from the figures as they stand.

A comparison of the amount of ready-formed fat in the food, with that of the determined or estimated total fat stored up in the increase of the respective lots of animals, showed that, even supposing the whole of that consumed had been retained, there remained from two-thirds to nine-tenths of the total amount stored up to be otherwise accounted for. It must have been produced within the body.

The next question was, whether this large amount of produced fat could possibly have been derived from the nitrogenous constituents of the food? or whether it must of necessity have had its source, in greater or less proportion, in the carbohydrates at the same time supplied?

Deducting from the total amount of nitrogenous substance consumed, the small amount estimated to be stored up as such in the increase of the animal, there remained a large proportion available, it may be, for the formation of fat, with other products. In order to give to the nitrogenous substance of the

food not stored up, its fullest possible (and even more than its fullest) value for fat-formation, the whole of its carbon, *minus* that which its nitrogen would require to form urea, is, for the sake of illustration, assumed to be available for fat-formation.

So calculated, the result in experiment 1, and also in two of the other cases in which the proportion of nitrogenous to non-nitrogenous substance in the food was considerably higher than is recognised by experience as the most suitable in the fattening food of the pig, was that more nitrogenous substance was available for fat-formation than was necessary to supply the estimated amount of produced fat. In the cases in which the nitrogenous substance was not so excessive, but still more than is the most appropriate, there was a considerable proportion of the total produced fat which could not possibly have been derived from the nitrogenous substance of the food. Lastly, when the proportion of the nitrogenous to the non-nitrogenous substance in the food was the most appropriate for fattening, there was a much larger proportion (about 40 per cent.) of the total produced fat, which could not possibly have had its source in the nitrogenous substance consumed.

Striking as are these results, it is obvious that a still larger proportion of the produced fat would appear to be formed from the carbo-hydrates, if it were assumed, with Henneberg and Voit, and as is doubtless nearer the truth, that 1·00 parts of albumin will not yield more than 51·4 parts of fat, instead of, according to the foregoing illustration, about 61 parts.

It will be well, however, briefly to consider, whether an amount of error in the estimates, which would turn the scale, and show that the whole of the produced fat might be derived from the nitrogenous substance of the food, is at all conceivable, at any rate in the cases in which the proportion of the nitrogenous to the non-nitrogenous constituents consumed was the most nearly that which is recognised as the most favourable for pig-fattening, and in which the largest amount of formation from the carbo-hydrates is indicated.

Obviously, the most important point to consider is the range of error admissible in the estimation of the fat stored up in the increase of the animal.

It would be necessary to reduce the estimate of the amount of fat stored up by more than 30 per cent. to bring it low enough to be covered by the fat in the food, *plus* that derivable from the transformed nitrogenous substance, leaving all the other calculations the same. If, however, we were to assume that 100 nitrogenous substance yielded only 51·4 fat, it would be requisite to reduce the estimate of the fat in the increase by more than 40 per cent., to reverse the indication. This is on the assumption that the whole of the fat of the food was stored up in the animal, which would certainly not be the case. It is also on the assumption that the whole of the nitrogenous substance of the food, not stored up as such in the increase, was digested, and available for transformation into fat, &c., but this again is certainly not the case. According to our own experiments, it may be supposed that, with a pig feeding exclusively on good barley-meal, about one-sixth of the total nitrogen voided would be in the fæces. But if it be assumed, according to the estimates of E. Wolff[1], that 20 per cent. of the nitrogenous substance, and 32 per cent. of the fat of the barley, would be voided undigested, and therefore without contributing to the deposition of fat, our estimate of the amount of fat stored up in the increase would have to be reduced by more than 55 per cent., or considerably more than half, to bring it within the amount derivable from the resorbed fat, and the transformed nitrogenous substance of the food.

It is submitted that a range of error in our estimates, at all approaching even the lowest of those above assumed for the sake of illustration, is simply impossible. It is further submitted, with the utmost confidence, that such is the wide margin in the case of pigs fattening rapidly on their most appropriate fattening food, that the question of whether or not the carbo-hydrates contribute to fat-formation may be conclusively settled by a properly conducted experiment with those animals, without any analysis of the fæces or the urine, or any determination of the products of respiration. To this end, we would suggest that two animals be selected, of a breed of good fattening quality, and as nearly as possible alike in characters and in weight. A convenient size and weight would

[1] *Landwirthschaftliche Fütterungslehre*, Appendix, Table I.

be, say about 90 lbs. per head. Let each be fed with ground barley of good quality, giving it, by degrees, as much as it will consume, until both weigh about 100 lbs. Then slaughter one, and determine its total amount of nitrogenous substance, fat, &c. Feed the other in the same way, that is with barley-meal (and water) exclusively, as much as it will consume, until it reaches about 200 lbs. in weight. Then slaughter and analyse it, as the first. The quantity and composition of the food must, of course, also be determined. Such an animal would consume somewhere about 500 lbs. of barley, more or less, and increase from 100 lbs. to 200 lbs. in live-weight, in from 8 to 10 weeks, more or less, according to quality of the animal, quality of the food, &c. &c. It is desirable that the animals selected should have been feeding on fairly good food previously, so that the transition to full fattening food should not be too sudden. It is also, of course, desirable, that the experiment should be made in duplicate if possible.

But, independently of the results of any such experiments, it may be asked, what is the lesson of common experience in this matter? We say, unhesitatingly, that the experience of the feeding of animals fully confirms our view.

In reference to this point we would call attention to the coloured diagrams Pl. XXII. which show the proportions of nitrogenous substance (black), of non-nitrogenous substance (yellow), and of total organic substance, nitrogenous and non-nitrogenous together (blue), respectively:—

I—consumed per 100 lbs. live-weight per week,

II—consumed to produce 100 lbs. increase in live-weight,

in the case of thirty different feeding experiments with pigs, each of which comprised not less than three and some four animals, and in each of which they fixed their own consumption[1]. That is to say, various current foods, but containing widely different percentages of nitrogenous substance, being selected, one (or a mixture) of high, or of medium, or of low

[1] "Pig Feeding;" *Jour. Roy. Ag. Soc. Eng.* Vol. XIV. Part 2; Experiments 1—8, and 12, Series 1; Experiments 1—12, Series 2; Experiments 1—5, Series 3; also "On the Equivalency of Starch and Sugar in Food," *Report of Brit. Ass.* for 1854; Experiments 1—4. See also "Experimental Enquiry into the composition of some of the Animals fed and slaughtered as human food." *Phil. Trans.* 1859, Part 2.

percentage of nitrogen, was given, *ad libitum;* or a fixed quantity of one or more was given, and another given *ad libitum;* and so on. In this way the animals fixed their own consumption, and from the results it may be judged by what requirement this was guided.

First, as to the consumption by a given live-weight within a given time; which of course met the collective requirements for both sustenance and increase. Diagram I illustrates this point. The lowest amount of nitrogenous substance so consumed in any one of the thirty experiments is taken as 100; and it is seen that the amount of it consumed ranged, among the thirty dietaries, from 100 parts to more than 300; and it averaged more than 200. Reckoned in the same way, the consumption of non-nitrogenous substance varied from 100 to only 177 parts, and averaged only 141 parts. Again, reckoned in the same way, the consumption of total organic substance (nitrogenous and non-nitrogenous together) ranged from 100 to only 150 parts, with an average of 125 parts.

Secondly, as to the amounts consumed to produce 100 lbs. increase in live-weight. Diagram II shows that, for this result, the consumption of nitrogenous substance ranged from 100 to 282 parts; and it averaged 173 parts. That of the non-nitrogenous substance ranged from 100 to only about 140 parts, with an average of 124 parts; and that of the total organic substance (nitrogenous and non-nitrogenous together) from 100 to only 147 parts, with an average of 122 parts.

It should be explained that, as in the Tables and Diagrams given in the original papers above referred to, the *total* amounts of nitrogenous and of non-nitrogenous substance, in the different foods, are taken as the basis of the calculations; no deduction being made for "indigestible" matter; nor is the fat in the food reckoned at any higher value than the other non-nitrogenous constituents. This plan was adopted as best representing the facts actually determined by analysis; but attention was at the same time directed to the varying amounts of indigestible matter in the different foods, and to the greater or less amounts of fat which they contained. We have, however, quite recently recalculated the whole of the experiments, making deduction for indigestible or undigested matter, according to E. Wolff's

Table already quoted, and with him multiplying the amounts of fat by 2·5, and have constructed Diagrams according to the data so obtained. These still more strikingly illustrate the point in question than the Diagrams herewith given; that is to say, they show a wider range in the amounts of the nitrogenous substance consumed in the different experiments, a less variation (excepting in one case in which there was much fat) in the amounts of the non-nitrogenous substance consumed, and especially a less range in the amounts of the total organic substance consumed. The two methods of calculation show, however, in most of the cases, much less difference in the relation of the nitrogenous to the non-nitrogenous constituents than might have been anticipated. With this explanation, we still adhere to our original plan of calculation, rather than adopt corrections based upon factors as yet not sufficiently established[1]. At the same time, we repeat that the points here indicated should be considered in judging of the results as they stand.

It is then perfectly clear, that neither the amount of food consumed in relation to a given live-weight within a given time (which of course covered the requirements for increase as well as sustenance), nor the amount taken to yield a given amount of increase in live-weight (which in its turn covered the requirements for sustenance also), was at all in proportion to the amount of the nitrogenous constituents it supplied. It is quite obvious, that the consumption, both for sustenance and for increase, was much more nearly in proportion to the amount of digestible non-nitrogenous constituents supplied; but it was more nearly still guided by the amount of the total digestible organic substance—nitrogenous and non-nitrogenous together—which the foods contained.

That the great variation in the amount of nitrogenous substance consumed was not due to a deficiency of it in most of the foods employed, is shown by the fact that it was in the experiment in which the food contained the lowest proportion of it, that the smallest amount of nitrogenous matter was not only consumed in relation to a given live-weight within

[1] Professor Emil Wolff has recently determined the proportions undigested of the different constituents of cocoa-nut cake, barley-meal, maize-meal, and pea-meal, in actual experiments with pigs. *Versuchs-Stationen Organ.* Band XIX. No. 4, 1876.

a given time, but was required to produce a given amount of increase. It is obvious, that where two or three times as much nitrogenous substance was consumed, it was much in excess of the normal requirement. In fact, the animals consumed almost regardless of the amount of nitrogenous substance supplied, until they had obtained a sufficiency of non-nitrogenous, or of total organic substance. It is further obvious, that the range of variation in the amounts of non-nitrogenous constituents consumed would have been very much less, but for the very variable amount of nitrogenous substance necessarily taken with it, the variable amounts of fat in the foods, and the greater amount of indigestible matter in some of them than in others. The indication is, indeed, that the excess of nitrogenous substance consumed substituted a certain amount of non-nitrogenous constituents; that, in fact, within certain limits, the two classes of constituents may, for the purposes of respiration and fat-formation, mutually replace each other.

Lastly on this point, not only did neither the amount of food consumed, nor the amount of increase in live-weight yielded, bear any relation to the amount of nitrogenous substance supplied, but the more excessive the supply of it the greater was the tendency to grow, and the less the tendency to fatten. There is, of course, a point below which the proportion of nitrogenous substance in the food should not be reduced; but if this be much exceeded, the proportion of the increase, and especially of the fat-increase, to the nitrogenous substance consumed, rapidly decreases; and it may be stated generally, that taking our current fattening food-stuffs as they are, it is their supply of digestible non-nitrogenous, rather than of nitrogenous constituents, which guides the amount, both of the food consumed, and of the increase produced, by the fattening animal.

In conclusion, we repeat that, in many of our experiments with pigs, much more fat was produced than could possibly have been derived from the albumin of the food, and hence the carbo-hydrates must have contributed directly to its formation; further, that experience in practical feeding is entirely in accordance with our views on the point.

THE INFLUENCE OF SALICINE ON THE HEALTHY BODY WITH SPECIAL REFERENCE TO ITS INFLUENCE ON THE TEMPERATURE. By Sydney Ringer, M.D., *Professor of Therapeutics at University College;* and J. S. Bury, *Physicians' Assistant at University College Hospital.*

In March, 1876, Dr Maclagan, of Dundee, strongly recommended Salicine in acute rheumatism; and in the following April Dr Senator, of Berlin, recommended salicine as a substitute for salicylic acid. As salicine is now largely used to reduce the temperature of febrile diseases, we were induced to undertake a series of observations to ascertain its effect on the temperature in health. Whilst making these experiments we noted carefully, at the same time, the effect of the drug on the various functions of the body; and in this paper we record the results. Before giving our experiments in detail we here point out the results of our observations.

Salicine, as has been pointed out by other observers, acts very much like quinia. Like it, in even large and toxic doses, as large as can be given with safety, salicine depresses the healthy temperature, but in a slight degree, and only for a brief period. Moreover this slight effect follows only the few first doses, and then, in spite of the continued administration of the drug, the temperature quickly recovers its original state.

The slight effect produced by salicine or quinia is well exemplified in the following tables:

Effect of Salicine on Temperature and Pulse.

Boy aged 10.

Dose.	Temperature depressed.	Depression lasted.	Pulse rose to.	Respiration.
30 grains	0.2	65 min.	Unaffected.	Unaffected.
30 „	no effect		„	„
60 „	0.8	about 2 hrs.	„	„
		Quinia.		
		Boy aged 10.		
10 „	none			
10 „	0.2			
10 „	none			
		Girl aged 13.		
8 „	0.2		94	
10 „	none		72	
10 „	none		72	
20 „	0.1	3 h. 15 min.	120	
20 „	0.4	45 min.	98	

These doses of quinia produced marked symptoms of cinchonism. These tables show that like quinia doses of salicine large enough to produce toxic symptons exert a very slight control over the healthy temperature. The above table regarding quinia is abstracted from a paper published by one of the authors and Mr Gill in the *Medical Times and Gazette.*

In this investigation when a sudden fall, which in a short time is recovered from, occurred in the temperature, we have considered the depression due to some accidental cause as cooling the mouth by exposure or cold drinks, &c., and have not used such observation in our calculations in this paper.

In order to produce any symptoms characteristic of the drug, a single large dose of one dram or more is necessary, or thirty grains repeated hourly, two or three times. Given less frequently, or in smaller doses, it induces no symptoms whatever. Toleration of the drug is soon established, so that at last large doses fail to produce any characteristic effect; though when given at first, without any graduation, these full doses, even after their discontinuance, produce very decided symptoms, which may persist one or two days, and may even become intensified the day after the withdrawal of the medicine. The repetition of large doses may produce slight fever, shown in delaying and greatly lessening the evening normal diurnal fall—an effect probably due to irritation of the stomach.

The aspect of a patient under full medicinal doses is rather characteristic, being in many respects similar to that of a person suffering from cinchonism. The expression is dull and heavy, the face quickly flushes on slight excitement, and the eyes become suffused. The flush, of rather a dusky hue, suffuses itself uniformly over the whole face. The patient, made more or less deaf, often complains of noises in the ears. He complains, too, of frontal headache, and his hands, when held out, tremble a little. His breathing is rather quickened and deepened. In some cases one symptom may predominate; thus deafness may be almost complete, without headache or muscular trembling; but it rarely, if ever, happens that any symptom is unaccompanied with the dull heavy aspect and the readiness to flush.

Under toxic, but not dangerous doses, the headache is often

very severe, so that the patient buries his head in the pillow. There may be very marked muscular weakness and tremor, associated with great muscular irritability, so that a slight tap, say on the shoulder, causes muscular contractions so strong as to jerk the arm backwards. There are often slight spasmodic twitchings when a limb is raised. Tingling of the extremities or other parts of the body sometimes occurs. The voice may become thick and husky. The respiration is hurried, sometimes deepened, sometimes sighing and shallow and almost panting, and seems as though it were performed rather laboriously, but the patient does not complain of any difficulty of breathing. The costal as well as the diaphragmatic movements are involved in the exaggerated breathing. Large doses, often repeated, quicken the pulse to 140 per minute, and it becomes very weak. In these healthy lads the drug did not cause delirium.

It is very noteworthy that salicine renders the sweat neutral or alkaline. We think, too, that the urine becomes neutral or less acid; but on this point our observations are too few to justify our speaking confidently. The alkaline reaction of the sweat we noticed in many rheumatic patients under the influence of large and frequent doses, and the sweat may be alkaline, whilst the urine is acid.

We find that if moderate doses are first given, the medicine may then be increased, till a lad ten years old, beginning with 80 grains, may be brought to take 180 grains daily, without any symptoms.

Though the effect of the drug on the temperature was so slight, we have introduced the charts, because, the observations being made with very great care and at less intervals than in any other observations we know of (excepting some other experiments made by one of the authors and read before the Royal Society), they are, on physiological grounds, valuable as indications of the course the temperature runs throughout the day and the effect on it of food, &c. Moreover on many days no salicine was given.

We tested the effects of salicine in three sets of experiments, each on three healthy lads. To the first two we gave large doses and produced decided symptoms; to the third we

gave at first smaller doses and increased them gradually till he took three drams daily, producing, as we shall see, scarcely any symptoms.

In two sets of experiments the temperature was taken under the tongue; in the other series, in the rectum. These lads took breakfast between six and seven; dinner between twelve and half-past, and tea between four and five.

We took the temperature hourly, from 9 a.m. till 12 p.m. Observations were made hourly for six days on the first lad; on the second for eight days; on the third for thirty days. For a few days we gave no salicine, that we might compare the temperature of the body on salicine days with non-salicine days.

Our first set of experiments were made on a lad aged ten, weighing 44½ lbs. His temperature was taken under the tongue and during the investigation, he was kept in bed but was allowed to sit up in it. He was admitted with belladonna poisoning, but our observations were not commenced till some days after his complete recovery.

CHART I. MEMORANDA.

Boy aged 10. Weight, 3 st. 2½ lbs. Admitted with Belladonna poisoning Aug. 4.

August 7.

Hour.	Pulse.	Resp.	Remarks.
9	80	20	6 a.m. Breakfast—bread and milk. Thermometer kept under tongue for five minutes.
10	76	20	
11	74	20	9·30. Mug of milk.
12	76	22	12·30. Dinner—mutton, potatoes, rice, bread and milk. Good dinner. Patient kept in bed but allowed to sit up and move about.
1	76	24	
2·15	76	22	
3	76	24	
4	76	20	4·30. Tea—milk, bread and butter. Good meal.
5	72	24	
6	72	22	
7	72	24	7·30. Mug of milk.
8	76	22	
9	72	22	
10	70	16	
11	70	16	
12	68	16	

August 8.

Hour.	Pulse.	Resp.	Remarks.
9·15	88	28	7·30. Breakfast—bread and milk.
10	76	24	
11	72	24	11. Mug of milk.
12	72	24	12·30. Dinner—mutton, potatoes, greens, rice pudding, water. Good dinner.
1	78	26	
2·15	78	26	
3	78	24	

4	76	24	
5	80	26	5·30. Tea—milk, bread and butter, 1 egg.
6	76	24	
7	76	28	7·30. Custard tart and milk.
8	76	22	
9	88	24	
10	80	20	
11	72	18	
12	76	18	12·30. Mug of milk.

August 9.

9	78	22	7·30 a.m. Breakfast—bread and milk. 9 a.m. Amount of urine passed since 9 a.m. yesterday ℥ 22.
10	84	24	10 a m. Mug of milk.
11	80	28	
12	72	28	12·30 p.m. Dinner—mutton, potatoes, no greens, rice pudding, milk. Good dinner.
1	82	28	
2	82	28	
3	80	20	
4	82	24	4·30 p.m. Tea—milk, bread and butter, one egg. Good meal.
5	84	26	
6	88	22	
7	84	24	7·30 p.m. Mug of milk.
8	80	24	
9	72	18	
10	70	16	
11	70	16	
12	72	19	

August 10.

8·45	76	24	5·45 a.m. Breakfast—bread and milk. Good. 9 a.m.
9·5	76	24	Amount of urine passed since 9 a.m. yesterday ℥ 22.
9·20	76	24	9·45 a.m. *Took 30 grains of Salicine in ℥j of water.*
9·45			10·5 a.m. Thermometer in mouth 10 min.
10·5	74	20	10 a.m. Mug of milk. 10. Patient complained of a
10·30	76	20	bitter taste on taking the drug; almost directly after swallowing it, he felt sick and had hard work to keep from vomiting; the sensation of sickness soon passed off. He complained also of frontal headache.
10·50	72	24	10·50 a.m. *Took 30 grains of Salicine in ℥j of water.*
11·10	76	18	10·50—11·40 a.m. The second dose was followed im-
11·40	76	20	mediately by nausea, which soon passed off; then severe frontal headache came on, so bad that the boy shut his eyes, and buried his face in his arm (this was at 11·10); his face was also much flushed and the conjunctivæ slightly injected. Giddiness, too, experienced. At 11·40 these symptoms had almost left him.
12·5	76	24	12·30 p.m. Dinner—mutton, potatoes, rice pudding, milk. Good dinner.
1·10	80	26	
2			
3	76	24	3 p.m. Currant bun.
4	76	24	4·45 p.m. Bread and butter and milk. Good meal.
5	78	25	
6	80	22	5·45 p.m. Sponge cake.
7	82	24	7·30 p.m. Mug of milk and piece of custard.
8	78	24	
9	72	22	
10	68	20	
11	64	18	
12	66	16	

August 11.

8·45	80	24
9·30	76	22
9·40	76	24
10	76	24
10·15	72	22
10·30	72	
10·45	72	24
11	76	26
11·15	70	22
12	76	26
1	72	24
2·15	76	24
3	76	22
4		
5		
6		
7	80	24
8	76	24
9	76	24
10	68	18
11	68	18
12	68	18

7·30 a.m. Breakfast—egg and milk and bread and milk.

9 a.m. Quantity of urine passed since 9 a.m. yesterday ℥ 20.

9·40 a.m. 60 *grains of Salicine in* ℥ ij *water.*

9·52 a.m. Flushed. Complains of frontal headache.

9·55 a.m. Headache severe—frontal. Flushes readily. Dull, heavy, and apparently decided muscular weakness. Tingling, like pins and needles, in right ankle. 11·30. Mug of milk.

10·4 a.m. Pain only over left brow. Dull, heavy flushes.

10·7 a.m. Headache getting much better (pupils rather more dilated?)

10·15 a.m. Headache only over left brow. Is very dull. Says he feels rather sleepy. Decided muscular weakness. Answers questions slowly. Movement made his head worse. Lies in a semi-stupid state. Is generally very lively. Pulse certainly much softer. Twitchings of leg which he cannot control, and slight of muscles of arm. Lies generally with eyes closed.

10·30 a.m. In much the same state. Still twitchings. Very dull. Drowsy; lies with eyes closed. No headache. Still flushes very readily. Pulse little fuller and stronger.

10·40 a.m. Drowsiness and dulness not decreased, and still twitches. No headache. Still flushes readily.

10·45 a.m. Still very dull, with decided muscular weakness. Crying, but has no pain. Pulse recovered.

11 a.m. Less dull. No headache or other pain. Still flushes.

11·15 a.m. A little dulness only noticeable.

12 noon. The boy is lively; looks himself again.

12·30 p.m. Dinner—mutton, potatoes, bread, milk. Poor dinner.

4·30 p.m. Tea—bread, butter, milk, jam tart.

7 p.m. Milk and bread.

August 12.

9	76	24
10	76	24
11	80	22
12	76	24
1	80	20
2	80	24
3	80	24
4	68	22
5		
6	84	24
7	84	26
8	84	26
9	72	18
10	75	18
11	68	18
12	68	17

7 a.m. Breakfast—bread and milk and one egg.

9 a.m. Quantity of urine since 9 a.m. yesterday ℥ 20.

12 noon. Dinner—mutton, potatoes, mug of milk. Poor dinner.

4·30 p.m. Tea—bread, butter, milk, one egg. Good meal.

7 p.m. Milk and two ginger cakes.

11 p.m. }
12 p.m. } Bedclothes thrown off body and legs.

For the first three days he took no medicine, on the fourth we gave salicine in two doses, each of thirty grains, and on the following day a single sixty-grain dose. Observations were continued throughout the sixth day, although he took none of the drug.

The results of our observations are put into the following table:

	Maximum temperature of day.	Rise after dinner.	Rise after tea.	Evening fall begun.	Diurnal variation.	Average temperature of day.	
1st day	99.1	0.4	0	8	1.6	98.4	No salicine
2nd day	99.5	0.6	0.5	7	1.4	98.7	No salicine
3rd day	99.4	0.4	0.4	6	1.7	98.7	No salicine
4th day	99	0	0	9	1.7	98.3	60 grains in two doses
5th day	99.3	0	0.2	6	1.7	98.5	60 grains in one dose
6th day	99	0	0.2	9	1.9	98.2	No salicine

In respect to this table we must first remark that the rise after dinner and tea lasted a very short time, and we think that part of this rise was due to the warm tea; for after warm drinks we have found that the mouth temperature is often considerably raised, sometimes even to the extent of a degree, remaining so a quarter of an hour or even longer.

A reference to the above table might lead to the conclusion that the effect of salicine was inappreciable or nil, but a glance at the accompanying chart (Chart I.) will show that the drug produced a manifest effect. On the fourth day, after taking three observations at intervals of a quarter of an hour, it will be seen that we administered by the mouth thirty grains of salicine dissolved in water at 9·45, and another thirty-grain dose at 10·50. The medicine produced a decided though slight effect on the temperature. Thus throughout the day, the temperature remained more stationary than on non-salicine days. After the first dose there occurred a fall of 0·2° Fah.; during the next hour it rose 0·4 in spite of the second dose, and the maximum temperature of the day was attained at 11·40. Then instead of rising after dinner and tea, as on the previous non-salicine days, it slowly and continuously declined, so that at 8 p.m. it had fallen 0·4° Fah., then the diurnal variation commenced and amounted to 1·7° Fah. Thus the effect of the salicine on this day was to lower the temperature 0·2° Fah., and to prevent the rise after dinner and tea, effects very slight and unimportant. Next (5th) day, after three observations, we administered in one dose sixty grains of salicine dissolved in two ounces of water at 9·40 a.m. The temperature from this time gradu-

ally fell, reaching its maximum fall of 0·8° at 11, it then rose and had recovered itself at 12, and between 12 and 5 it rose 0·3°; the evening fall then began and amounted to 1·7° Fah. There was no rise after dinner, and only 0·2° after tea. Thus on this day the effect was a fall of 0·8°, lasting about two hours, and no rise after food. The amount of diurnal variation was unaffected on both the salicine days.

Next day he took no salicine, and his temperature remained remarkably uniform throughout the day, till the diurnal variation set in. The evening fall began between eight and nine, and the diurnal variation amounted to 1·9° Fah.

The drug produced no effect on the pulse or respiration.

Although on each of the two days we gave the same dose, the drug produced far more decided effects after the second than after the first dose. On the first day we gave two thirty-grain doses at sixty-five minutes interval; on the next day sixty grains were given at once. This difference would indicate that the drug is quickly eliminated.

The symptoms produced were slight nausea, probably due to the bitter taste of the drug; then, in a few minutes after the second dose, severe frontal headache set in, so severe that the lad shut his eyes and buried his head in his arm. Flushing of the face especially on any excitement. Slight injection of the conjunctiva, and giddiness. In an hour these symptoms had almost left him, a fact confirming the conclusion that the drug is speedily eliminated.

Sixty grains produced the same symptoms in a more marked degree. Severe headache and flushing came on in twelve minutes. Though a very lively boy, he became very dull and stupid, lying with his eyes closed, and answering questions slowly. He complained of tingling like pins and needles in his right ankle, and suffered from very decided muscular weakness, soon accompanied by muscular twitchings and tremblings of the legs and arms. At this time the pulse was much softer.

In the following table we give the time these symptoms set in and their duration, calculating from the time of taking the medicine.

	Set in.	Ceased.
Headache	12 min.	50 min.
Flushing	12 min.	1 h. 20 min.
Muscular weakness	15 min.	1 h. 20 min.
Muscular twitchings	35 min.	1 h. 20 min.
Dullness and heaviness	15 min.	1 h. 45 min.

The quantity of urine was almost unaffected, as the following table shows:

	Daily amount.
Without medicine	22 oz.
" "	22 oz.
Salicine day	20 oz.
" "	20 oz.

The next series of observations were made on a lad aged nine, convalescent from pneumonia, his temperature having

become normal ten days previously. We experimented somewhat differently.

The boy was kept in bed. His temperature was taken hourly in the rectum. For two days he took no medicine; on the two following days he took salicine in thirty-grain doses at 10 a.m., 11 a.m., 2 p.m., 3 p.m., 5 p.m., and 6 p.m.; thus in the course of the day he took ʒiii. Next day we administered thirty-grain doses eight times (℥j.), at 10 a.m., 11 a.m., 12 p.m., 1 p.m., 2 p.m., 3 p.m., 4 p.m., and 5 p.m.

The results with this lad are rather singular. On the first day these large doses produced no symptoms, in fact symptoms did not set in till noon of the second day, but they increased during the night, after the discontinuance of the medicine, and were severe all next day, and for three days after.

As in the previous observations, we shall speak first of the effect of the salicine on the temperature, pulse, and respiration.

CHART II. MEMORANDA.

P. B. Aged 9. Convalescent from Pneumonia. Temp. normal on 9th.

September 19.

Hour.	Pulse.	Resp.	Remarks.
			5·30 a.m. Breakfast—bread and butter, one egg, mug of milk. Moderate breakfast.
9 a.m.	70	22	
10	80	24	10 a.m. Lunch—mug of milk and bread.
11	80	24	
12	80	28	12 noon. Dinner—mutton, potatoes, greens, pudding (rice), mug of milk. Moderate dinner.
1 p.m.	84	24	
2	80	26	
3	70	28	
4	72	28	
5	80	28	5 p.m. Tea—bread and butter, one egg, mug of milk, small bunch of (about 12) grapes. Good meal.
6	80	24	
7	74	24	
8	70	22	Profuse perspiration of face and upper limbs and chest; lower limbs dry.
9	66	22	
10	66	22	Face still moist; arms only slightly moist.
11	70	18	
12	70	18	

September 20.

Hour.	Pulse.	Resp.	Remarks.
			5·30 a.m. Breakfast—bread, one egg, mug of milk. Moderate breakfast.
9 a.m.	72	24	
10	68	24	
11	68	24	
12	72	20	12 noon. Dinner—mutton, potatoes, greens, milk, pudding (rice). Good dinner.
1 p.m.	68	24	
2			
3	70	24	
4			
5			4·30 p.m. Tea—bread and butter, one egg, mug of milk, and a few grapes.
6	70	24	
7	68	24	
8	68	24	Mug of milk at 7 p.m.
9	60	20	
10	62	20	
11	68	24	
12			

September 21.

			5·30 a.m. Breakfast—bread and butter, one egg, mug of
9 a.m.	72	26	milk. Good breakfast. Urine ℥ xviii. in last 24 hrs.
9·45			10 a.m. * *Salicine gr.* xxx. in water ℥ i. 10·15. No
10·15	68		headache, no heaviness, or any pain or uneasiness.
10·30	76	24	10·30. No symptoms.
11·15			11 a.m. *Salicine again given in same dose.* Boy was
11·30			repeatedly asked between 11 and 12 if he felt well, and
12·0	76	28	complained of nothing. No alteration in pupils or
1 p.m.	76	28	general aspect of face.
1·45			2 p.m. *Salicine gr.* xxx. *again given.* Bowels open
2·25	78	24	once. No symptoms.
3·15			3 p.m. *Salicine gr.* xxx. *repeated.*
3·45			
4·15			4·15 p.m. Tea—bread and butter, one egg, mug of
			milk, a few grapes. Very good meal.
5·15			5 p.m. *Salicine gr.* xxx.
5·45			No symptoms.
6·30			6 p.m. *Salicine gr.* xxx. *repeated.*
7·30			No symptoms.
8·30			
9·30			
11·0			
12·0			

September 22.

			5·30 a.m. Breakfast—bread and butter, one egg, mug
9 a.m.	88	24	of milk. Moderate breakfast.
9·45			10 a.m. *Took* 30 *grs. of Salicine in* 1 *ounce of water.*
10·15	88	28	No symptoms. Urine ℥ xiii. in last 24 hours.
10·45			Urine slightly acid; contains abundance of Salicine.
11·15			11 a.m. *Took* 30 *grs. of Salicine.* No symptoms.
			12 noon. *Another dose of Salicine.*
11·45			12·15. Dinner—small piece of mutton, little potato,
12·30			pudding, mug of milk. *Very poor* dinner. Bowels
			open 4 times.
1·15	104	32	1 p.m. * *Another dose of Salicine.*
1·30			1·40 p.m. Tremor of hands when held out. Face
2·15	108		flushed, perspiring; looks dull but complains of no
			headache or pain. Pulse large, soft, compressible.
			2 p.m. *Another dose of Salicine.*
3·0			3 p.m. *Another dose of Salicine.* 3·15. Much tremor
			of hands; face flushed.
3·30	112	32	4 p.m. *Another dose of Salicine.* } Face flushed.
4·30			5 p.m. *Repeated.* }
5·45	116	30	5·15 p.m. Tea—one egg, bread and butter. Very good
			tea. Marked tremor of the hands whilst eating.
			Grasp of hands strong and equal.
			9 p.m. Urine slightly acid. Sp. gr. 1028.
7 p.m.			
8			
9	112	28	
10			
11			
12	108	24	

September 23.

9 a.m.	112	32
10	124	32
11	128	36
12		
1 p.m.	140	40
2	128	32
3	124	33
4	120	30
5	116	32
6	116	32
7	116	32
8	116	32
9	108	26
10	104	24
11		
12	96	22

5 a.m. Boy vomited twice, bringing up remains of food. No breakfast.

9 a.m. Looks heavy and dull; is decidedly deafer; can only hear a watch tick when laid *on the ear.* He feels a tingling in the right ear near the surface; has no buzzing noises in head, no headache, nor pain anywhere. Does not seem to understand questions so well as formerly, and there is a little tremor of lips in speaking and the voice is thick. Breathing laboured and trunk shakes a little during the act. Hands tremble when held out, and small spasmodic movements of the whole upper limb occur at intervals. Also slight jerks and tremor of lower limb when raised from bed.

9·30 a.m. Feels sick but does not vomit. Grasp of hands is weaker than it was yesterday. Speech a little jerky; voice husky; words not well laid hold of, lips and tongue not being used with natural freedom. Eyes heavy and half shut. Mouth wide open. Rather thirsty. Pulse soft and compressible.

1·30 p.m. Urine neutral; abundance of Salicine. Great muscular irritability, on tapping the muscles they contract. Breathing a little laboured.

4·0 p.m. Pulse of better quality. Symptoms passing off; expression brighter; much less deafness; irritability of muscles as before. No pain anywhere. Manner still dull. Breathing less laboured: more thoracic than diaphragmatic. Much Salicine in urine.

8·0 p.m. Urine slightly acid, contains plenty of Salicine. Less irritability of muscles. Manner still dull, and boy heavy and sleepy.

Dinner at 12 noon of small chop, greens, and potatoes. A moderate dinner.

Tea at 4·15 p.m.—bread and butter, one egg, mug of milk with a little tea in. Very good meal.

September 24.

9 a.m.		
10	100	26
11	104	28
12		
1 p.m.		
2	108	24
3	108	28
4	94	
5	90	
6	90	
7	90	
8	90	
9	82	
10	82	
11	84	18
12		

5·30 a.m. Breakfast—bread and butter, one egg, mug of milk. Good breakfast.

10 a.m. Deafness less. Still looks dull, and unless spoken to, lies with eyes half closed, and very often is asleep.

Muscular irritability still present though less than yesterday, and the muscles contract when tapped. Urine as before.

3 p.m. Pulse still compressible. Breathing less laboured, but thoracic. Tremor of hands and arms when held out. Slight muscular irritability. Boy looks brighter, and can now hear a watch tick when held at a distance of four inches from the ear.

12 noon. Dinner—mutton, potatoes, pudding. Moderate dinner.

5·15 p.m. Tea—bread and butter, one egg, and mug of milk. Good meal.

September 25.

9 a.m.	74	22
10	72	24
11		
12	88	26
1 p.m.		
2		
3	100	
4	96	
5	100	24
6		
7	92	22
8		
9		
10	88	18
11		
12		

5·30 a.m. Breakfast—bread and butter, one egg, mug of milk. A good breakfast.

One stool at 3 a.m. and a small one at 8 a.m.

8·15 a.m. Boy looks much brighter, but his face is very pale. There is still a very little tremor of hands when held out, and just a trace of irritability in the back muscles. Less deafness; eyes less heavy-looking. Urine reaction as before, just tinging blue litmus red; about ½ inch in height in moderate-sized test-tube is coloured deep purple with 1 drop of Liq. Ferri Perchlor.; the colour dissolves on shaking, but 1 drop more of L. F. P. produces a permanent colour.

4 p.m. Urine as before. Very slight tremor of hands. Can now hear watch tick when held 1 or 2 feet from head.

1 p.m. Another stool, making 3 to-day.

12 noon. Dinner—very small piece of mutton and rice pudding. A very poor dinner.

4 p.m. Tea—bread and butter, one egg, and mug of milk. A good meal.

September 26.

9 a.m.	88	22
10	76	22
11		
12	88	20
1 p.m.		
2		
3		
4	84	24
5		
6	84	22
7		
8		
9		
10	84	16
11		
12		

5·30 a.m. Breakfast—bread and butter, one egg, mug of milk.

9 a.m. Free from dulness and deafness, can hear a watch tick at a distance of 3 feet from head, an improvement even on yesterday. No tremor or muscular irritability.

Urine slightly acid, contains Salicine, but reaction not quite so marked as before.

4 p.m. Urine, passed 10 minutes since, is neutral; contains dense white pp. of phosphates; slight purple colour produced with 2 drops of L. F. P., showing a trace of Salicine still present.

12 noon. Dinner—mutton, potatoes, greens. A poor dinner.

4 p.m. Tea—bread and butter, one egg, and mug of milk. A good meal.

The chart (Chart II.) which we have given will show that on the first day the temperature rose between 9 a.m. and 1 p.m. $\frac{9}{10}$° Fah. and then slowly fell; the diurnal variation apparently beginning about 6 p.m. and amounting to 2·9° Fah. Next day, also without salicine, the course of the temperature was very singular. It remained pretty stationary from 9 a.m. till 1 p.m. and then fell 1°, remaining about this point till 9 a.m. and again fell 1·6°; the diurnal variation amounting to 2·3°. Next day, the first on which salicine was given, the temperature fell after the first dose of 30 grains ·4° in 1½ hour, and remained depressed for about 3 hours, and then rose to its original height in spite of the continuance of the medicine. The evening fall began at 7·30 p.m. and the diurnal variation amounted to 1·9° Fah. The only effect, therefore, of the salicine was a very slight and temporary depression of the temperature, not maintained by the continuance of

the medicine, and the diurnal fall was not quite so great as on the two previous days, though within the limits of variation of health.

Next day when 3 drachms of salicine in divided doses was given the temperature was not even temporarily depressed; in fact it rose ·6° between 9 a.m. and 1 p.m., and then slowly fell ·3° till 3.30 p.m. The evening fall began between 7 p.m. and 8 p.m., and the diurnal variation amounted to 1·5°.

Next day, with very marked symptoms, though without salicine, the temperature ran the same course, rising gradually from 9 a.m. till 1 p.m., and after 4 p.m., slowly falling till 12 p.m.; the daily variation amounting to only 0·9°. On these two days the only apparent effect therefore of salicine was to lessen the diurnal range, with a very slight increase in the maximum temperature of the day; and, strange to say, these effects were marked most on the day following the large doses of salicine, not on the day the large doses of salicine were taken, but on the following day.

Next day, taking the temperature as usual, it remained pretty stationary, varying only ·2° from 9 a.m. till 6 p.m. and then fell, the diurnal variation amounting to 1·8°.

On the two days following the temperature returned to the course it observed on the first non-medicine day, slightly rising from 9 a.m. till 1 p.m., the rise amounting to 0·5° Fah., and then the diurnal fall began respectively at 7 p.m. and 6 p.m. and amounted to 2·2° and 1·7°.

We now summarize our observations in the following table:

Date.	Medicine given.	Amount.	Maximum temperature of the day.	Amount of diurnal variation.
Sep. 19	None		99.1	2.9
„ 20	None		98.9	2.3
„ 21	Salicine	ʒ iii	98.9	1.9
„ 22	Salicine	℥ j	99.3	1.5
„ 23	None		99.5	0,9
„ 24	None		99.4	1.8
„ 25	None		99.5	2.2
„ 26	None		99.5	1,7

We may remark that in these observations, taken in the rectum, very little and generally no rise of temperature occurred after food—a circumstance strongly favouring a previous suggestion, that the rise after food, in cases where the temperature is taken under the tongue, is due to the hot food heating the mouth by direct contact.

This table, coupled with preceding observations, shows that even very large doses, as large as can be safely given, depress the temperature very little, and only after the first few doses, and subsequently, instead of lowering the temperature, the drug produces slight fever; thus it slightly raised the temperature, though not above the limits of health, but delayed the onset of the evening fall, and lessened the amount of diurnal variation, thus giving evidence of the febrile movement. This slight fever may, we think, be due to catarrh of the stomach, caused by the medicine, which, in so many instances excites vomiting.

In this case the pulse and respirations were greatly affected, both being considerably quickened. As was the case with the temperature, so with the pulse and respiration, the effects of the medicine were most marked the day after the discontinuance of the drug. Thus the full effects as regards the pulse and respirations and other symptoms culminated about 1 p.m. on the day following the withdrawal of the drug, the pulse at that time being 140 and the breathing 40. On the following day, that is, two days after the administration had ceased, the pulse and respirations had greatly fallen, but were still quick and next day they became normal. The pulse when frequent was very compressible, but improved in quality as it diminished in frequency.

The drug's influence on the pulse and respiration is shown in the following table:—

Date.	Medicine.	Amount of Medicine.	Maximum and minimum pulse of the day.	Maximum and minimum respiration of the day.
Sep. 19	None		66 to 84	18 to 28
„ 20	None		68 to 72	20 to 24
„ 21	Salicine	ʒ iii	68 to 78	24 to 28
„ 22	Salicine	℥ j	88 to 116	24 to 30
„ 23	None		112 to 140	22 to 40
„ 24	None		82 to 108	18 to 28
„ 25	None		72 to 100	18 to 26
„ 26	None		76 to 88	16 to 24

We now give a resumé of his symptoms. Nothing was noticed till noon of the second salicine day until the boy had taken in all ʒv. of the medicine. Between one and two we noticed that his face was flushed and he looked dull, and that there was some tremor when his hand was held out. In the evening the tremors were more marked. At 5 a.m. the following day he twice vomited. On this day though he had discontinued the medicine since five o'clock the previous evening, his symptoms were very marked and for the most part of the same characters as in the other lad,—namely dulness, so that he did not seem very well to understand questions; deafness; tingling in the right ear; slight tremor of the lips on speaking and thick husky voice; breathing rather laboured; trembling of hands when held out; slight spasmodic movements of the upper limbs; slight jerks of the lower limbs when they are raised from the bed; grasping power weaker than before; much irritability of the muscles on percussion; but strange to say he never complained of headache nor buzzing. These symptoms were at their height at midday, and were so marked and the pulse and respirations so quick, that we must confess we felt a little relief when the toxic symptoms, which became far more marked than we had expected, abated, not that at any time the boy was dangerously ill, but as the symptoms progressed, after discontinuing the medicine, we did not know how long and to what degree they might increase.

Next day, that is, forty-one hours after the last dose of medicine, he was still deaf, though less so, and was dull and unless spoken to lay with his eyes half closed, and very often fell asleep. Muscular irritability had diminished and the hands and arms trembled when held out: the pulse was still compressible. Even sixty-five hours after the last dose he was still dull, rather deaf, and there was slight tremor of the hands and irritability of percussed muscles.

Next day he had quite recovered. We tested the urine frequently for salicine and found some even 95 hours after the last dose.

In our third series of observations on a lad aged ten, and weighing 64 lbs., we experimented in a somewhat different way. We took the temperature under the tongue every three hours. For three days we administered no medicine; on the following twenty-six days we gave salicine in increasing doses, at first in 20 grain (80 grains daily), and latterly in 30 gr. doses several times daily, till he was taking in divided doses 180 grains daily. The boy got up and spent the day about the ward.

We put our observations into the following table :

	Medicine.	Maximum temperature of day.	Average temperature of day till 9 p.m.	Average till 12.	Diurnal variation to 9 p.m.	Diurnal variation to 12 p.m.	Highest pulse of the day.
1st day	None	99.2	98.66		1.1		84
2	,,	99	98.64		1.2		80
3	,,	99	98.6		1.2		84
7th day	80 grs.	99.1	98.7		1.1	1.9	88
8	,,	99.2	98.8		1.4		96
9	,,	99.2	98.7	98.4	1.4	2.2	92
10	,,	98.8	98.3	98.12	1.0	1.6	88
11	120 grs.	99.4	98.8	98.5	1.3	1.8	92
12	,,	99.4	98.86	98.81	1.3	1.8	96
13	,,	99.3	98.96	98.78	0.9	1.4	100
14	100 grs.	99.2	98.6	98.5	1.0	1.4	96
15	120 grs.	99.2	98.62	98.60	1.0	1.3	
16	,,	99.3	98.75	98.62	1.2	1.4	96
17	,,	99.4	98.48	98.32	1.9	2.2	100
18	,,	98.8	98.22	98.05	1.4	1.6	92
19	,,	99.3	98.66	98.51	1.3	1.5	88
20	100 grs.	99.2	98.7	98.5	1.1	1.7	
21	150 grs.	99.3	99.06	98.78	1.1	1.9	88
22	,,	99.3	98.81	98.67	0.6	1.5	92
23	,,	99.6	98.94	98.68	1.5	2.2	96
24	,,	99.4	98.88	98.63	1.9	2.0	
25	175 grs.	99.2	98.68	98.41	1.5	2.2	96
26	150 grs.	99.2	98.9	98.73	1.2	1.8	100
27	180 grs.	99.3	98.91	98.71	0.9	1.8	96
28	,,	99.5	99.05	98.82	1.1	2.0	96 [bath
29	,,	100.2	99.36	99.1	2.1	2.7	Had hot air
30	,,	99.5	99.11	98.91	0.7	1.8	100
31	30 grs.	99.4					
32	None	99.7	98.84	98.60	1.7	2.3	100

The preceding table (and charts which we think it unnecessary to publish) shows that these large doses of salicine had no appreciable effect on the temperature. It is true that on one day the temperature rose to 100°; but that occurred during the use of the hot air bath, employed to produce sweating, that we might test the reaction of the sweat; on the other hand the pulse was a little quickened. On the fifth day of taking salicine he complained of slight deafness, and on the tenth day it is noted that the deafness had a little increased, but two days afterwards it had disappeared. Beyond the influence on the pulse and hearing, the medicine produced no apparent effects, the boy eating well, sleeping well, and indeed appearing in all respects quite well.

THE CRANIAL OSTEOLOGY OF AMIA CALVA. By T. W. Bridge, B.A., *Trinity College, Demonstrator of Zoology and Comparative Anatomy in the University of Cambridge.* (Pl. XXIII.)

The cranial osteology of living Ganoids has been hitherto but partially investigated; and even those genera that have been described by the older anatomical writers will abundantly repay renewed investigation now that the researches of Parker, Gegenbaur, and Huxley, have thrown so much light upon the morphology of the Vertebrate skull.

Agassiz[1], it is true, has given to us an elaborate account of Lepidosteus, and the earlier description of Polypterus by H. Müller[2] has been supplemented by Dr Traquair's[3] opportune paper; while to Dr Günther[4], and Prof. Huxley[5], we are indebted for exhaustive accounts of the skeleton of Ceratodus.

On the other hand, I am not aware that, beyond the more or less brief accounts to be found in Joh. Müller's *Vergleichende Anatomie der Myxinoiden*[6], we have any detailed descriptions of Spatularia, Acipenser or Amia; and the anatomical student who may wish to acquire any complete knowledge of these genera must content himself with the above-mentioned references, or with such facts as he may be able to glean from such anatomical text-books as Huxley's *Manual of Vertebrata,* Owen's *Comparative Anatomy,* or the *Grundzüge der Vergleichenden Anatomie* of Gegenbaur.

More especially is this true of Amia. The zoological characters of this genus have been described by several zoologists. Vogt[7] first detected its true position among the Ganoids, and removed it from the Clupeoid Teleostei with which it had been placed by Müller[8]; and Hyrtl[9] and Franque[10] have described

[1] Agassiz, *Poiss. Foss.* Tom. II.
[2] *Abhandl. Ak. Wiss. Berlin,* 1844.
[3] *Journal of Anatomy,* Vol. IV.
[4] *Phil. Trans.* 1871.
[5] *Proc. Zool. Soc.* 1876.
[6] *Vergl. Anat. d. Myx. Berlin,* 1835.
[7] *Annales des Sciences Naturelles,* Tom XXIV. Heart and Alimentary Canal figured.
[8] Müller's paper "Sur les Ganoïdes et sur la classification naturelle des Poissons" is translated by Vogt in the XXV. Vol. *Ann. Sc. Nat.*
[9] *Ak. Wiss. Wien,* 1855.
[10] *Amiae calvae Anatomia,* Berlin 1847.

the generative organs and visceral anatomy. But, I am not aware that there exists any connected account of the osteology of the skull of this genus, or that the skull has been figured. As I have lately had the opportunity of dissecting a full sized specimen of Amia calva, and as several interesting facts were elucidated which I have never seen mentioned in any of the text books, or anatomical memoirs on the Ganoids, I have ventured to give the following description of its skull.

Ganoid plates and membrane bones of the cranium. (Figs. 1 and 2.)

The flattened and depressed cranium is invested externally by a series of ganoid plates, all of which are firmly attached to the underlying cartilage by means of the osseous lamina adhering to the under surface of each ganoid plate. The external highly polished surfaces of the plates, with the exception of the nasals and the dermo-ethmoid, are destitute of any covering of soft skin, and all of them have their surfaces sculptured into wavy and branching rugosities, which radiate from the centre towards the circumference of each plate.

Viewed from above (fig. 1) the following bones are seen. Overlying the occipital region there is, as in many of the Siluroidei, a large square dermo-supra-occipital (*d.so*). This bone rests upon the subjacent cartilage of the occipital region of the chondrocranium, and by its hinder margin upon the epiotics; laterally it articulates with the two parietals, in front with the hinder edges of the frontals, while posteriorly it is in contact with the supra-temporals. Owen[1] says that this bone is divided by a median suture, but in my specimen there was no trace of such a suture. The dermo-supra-occipital is flanked on either side by a bone which overlies the pterotic region of the otic capsule, and occupies much the same position in Amia as the bone marked "Pa. Ep." in Huxley's[2] figures of Clarias, and the bone usually called dermo-epiotic in many Siluroids. I shall call this bone parietal, though I am not sure that it would not be better to call it 'dermo-pterotic,' or 'dermo-epiotic.'

[1] *Comparative Anatomy*, Vol. I.
[2] Essay on the Classification of the Devonian Fishes, *Mem. Geol. Survey*, Dec. 10. Figs. 21, 22.

Each parietal (*pa*) is triangular in shape, with straight external and posterior margins, but articulating by a sinuous internal edge with the dermo-supra-occipital and frontal bones. Its base is in contact with the supra-temporal, and its apex with the dermo-sphenotic. Each parietal, like most of the other investing ganoid plates, has its under surface much thickened by an adherent parostosis, which, along the outer margin of the plate, is produced downwards into a short vertical ridge, which rests upon the pterotic region of the subjacent cartilage, and upon the opisthotic. This vertical plate prevents the horizontal portion of the parietal from resting directly upon the cartilage, and consequently, when the skull is viewed from behind, a vacuity is to be seen bounded by the horizontal and descending plates of the parietal, the epiotic and the cartilage of the cranial roof. The outer margin of each parietal fulfils the function of a supra-temporal in transmitting the cephalic continuation of the main lateral slime-canal.

The two supra-temporals (*s.tp*) are triangular bones with their apices pointing inwards towards each other, but not coming into contact; behind they overlap the post-temporals (*p.tp*). Each is pierced by the main lateral slime-canal in its passage forwards to the parietal, and, in addition, each is traversed by the transverse canal by which the two lateral canals of opposite sides are connected with each other. In Polypterus these two bones are represented by a chain of six transversely disposed ossicles, through each of which the transverse slime-canal passes, and a similar arrangement is found in Lepidosteus.

The frontals (*fr*) are the largest of the investing cranial bones; they cover the greater part of the cranial roof, extending from the sphenotics behind to the prefrontals in front, and as their width is much greater than that of the interorbital region of the cranium, they roof over the orbits. The frontals articulate with each other in the median line by an interdigitating suture; behind, they are in contact with the parietals and dermo-supra-occipital; and in front they articulate by a straight suture with the posterior margins of the nasals.

Small dermo-sphenotics (*pt.f*) overlie the true sphenotics and lie along the outer margin of each frontal; their anterior edges mark the posterior limits of the orbits. At the anterior and

external edge of each frontal there is a small dermo-prefrontal overlying the true prefrontal.

All the bones that have yet been described are obviously composed of an external ganoid plate, and of an internal and much thicker lamina resulting from the ossification of the subcutaneous tissue; but the ganoid plates, to be presently described, appear to be composed of the ganoid element only. The large paired bones (*na*) in front of the frontals, directly overlie the nasal capsules, and by their emarginate anterior edges bound the foramen for the anterior nares (*a.n*). These bones, at first sight, greatly resemble the paired dermo-ethmoids of Polypterus, but as the T-shaped bone in front of them appears to be the true dermo-ethmoid, I shall call these paired bones, nasals.

The outer margin of each nasal is in contact throughout its whole length with a long and slender præorbital bone (*p.orb*). There is a bone occupying much the same position in Clarias.

The dermo-ethmoid (*eth*) is somewhat T-shaped, with its anterior transverse part slightly concave from side to side. It overlies the prenasal process and the premaxillæ. Each end of the transverse part is in contact with the præorbital bone, while the stem of the T passes backwards between the nasals, separating them for about a third of their extent.

The orbit is bounded in front, below, and behind by a series of five orbital bones; as there are no supra-orbital bones the orbit is limited above by the frontal. A large lachrymal plate (*l*) bounds the orbit in front, and two very large wedge-shaped post-orbital bones (*pt.orb*), which extend backwards over the cheeks bound it posteriorly. These bones appear to be represented in Polypterus by a single large cheek-plate (marked *Y* in Dr Traquair's paper), which appears to have coalesced behind with the præoperculum. The lachrymal and postorbital bones are connected beneath the orbit by two small suborbital pieces (*s.orb*). All the orbital ganoid plates have their orbital margins much thickened by subcutaneous ossification.

Opercular bones. (Fig. 2.) As in the typical Teleostei there are four opercular bones. The preoperculum (*p.op*) is a narrow crescentic bone firmly anchylosed to the hyomandi-

bular and symplectic bones. The mandibular branch of the great lateral slime-canal traverses the whole length of the preoperculum, and gives off several short transverse branches in its course. There is a large operculum (*op*) articulating with the condyle on the hyomandibular, a small interoperculum (*i.op*) connected by ligament with the angle of the mandible, and wedged in between the two last-mentioned elements—there is a suboperculum (*s.op*).

In this specimen of Amia there were eleven branchiostegal rays. They increased in size progressively, and the uppermost one, which is the largest, is attached by a special articulation to a facet on the outer side of the epihyal. The rays are all attached to one side—the outer side—of the ceratohyal, and not to both sides as is commonly the case in Teleostei.

In comparing the skull of Amia with the skulls of certain of the Siluroidei, and notably with that of Clarias, it is interesting to notice that, in addition to the more obvious and less important points of resemblance between the two genera necessitated by the flattened condition of the head, and a foreshortening of the prefrontal region, there is a close agreement between them in the number and relations of their ganoid plates.

In Clarias, as in Amia, there is a median dermo-supraoccipital; there are also 'parietals' or dermo-epiotics, dermosphenotics, and dermo-prefrontals; paired frontals and nasals; and a median T-shaped dermo-ethmoid. The ethmoid is proportionally smaller, and the nasal proportionally larger in Amia than in Clarias, so that the ethmoid completely separates the nasals in the latter fish; but otherwise there is but little difference between the two forms in the disposition of their ganoid plates.

In Clarias there are also two large postorbital bones covering the cheeks and extending nearly to the preoperculum. This genus has supra-temporals and preorbitals, as in Amia.

The ventral surface of the cranium is invested by a parasphenoid and vomers.

The former bone (*pa.s*) extends along nearly the whole length of the base of the cranium, from the vomers in front to

the posterior margin of the basioccipital. Behind, this bone is somewhat spoon-shaped, and in front it partially separates the two vomers from each other. About the middle of its length the parasphenoid gives off two lateral wings (*a.p*), one on each side, which curve upwards in front of the prootic and between the foramina for the exits of the fifth and seventh nerves till they abut against the post-frontals. From the base of each lateral ala a small process is given off which unites with the descending process of the alisphenoid, and so forms the outer boundary of the canal through which the muscles of the eyeball pass.

The upper surface of the parasphenoid is marked by a longitudinal ridge, which is firmly adherent to the grooved inferior surface of the basi-occipital and the cartilaginous basis cranii. The lower surface of the bone is garnished with a number of closely set asperities.

The anterior third of each vomer (*vo*) is suturally united to its fellow; the posterior two-thirds are separated by the intervention of the parasphenoid. The vomers carry a number of closely set conical teeth arranged in a crescentic series parallel to those in the premaxillæ.

Premaxillæ and maxillæ. (Fig. 3.) Each premaxilla (*p.mx*) consists of an expanded and thickened marginal portion in which the long and curved teeth fringing the anterior margin of the gape are situated, and of an ascending portion which passes backwards beneath the nasals in contact with the subnasal cartilage and inter-nasal septum as far as the anterior edges of the frontals. The spoon-like upper surface of this ascending plate upon which the nasal capsules lie is perforated in the centre by an oval foramen for the passage of the olfactory nerve to the olfactory mucous membrane. In the median line between the two premaxillæ the prenasal process (*p.n*) becomes visible. Superiorly the premaxillæ are covered by the nasals and dermo-ethmoid.

The maxillæ (*mx*) are very Teleostean. Each bone carries a number of small, but sharp teeth, and each has its anterior end prolonged into an inwardly curved process which rests in a groove in the extreme anterior end of the palatine. The

maxillæ do not form any part of the orbital boundary. Upon the upper part of the hinder margin of each bone there is a jugal bone.

Chondrocranium and its Ossifications. (Figs. 2 and 3.)

When the investing parostoses and ganoid plates just described have been removed it is seen that the cartilaginous roof of the chondrocranium is complete, there being no trace of the fenestræ which exist in all the other Ganoids with the exception of Lepidosteus. The chondrocranium is very depressed and somewhat wedge-shaped, broad behind in the occipital region and tapering gradually to the prenasal process anteriorly. Neither the periotic nor the olfactory regions form very conspicuous lateral prominences. Internally the cranial cavity is broad behind, and with a gradual diminution in width and height is continued forwards between the orbits to a point between the prefrontals, where it is terminated by a lamina perpendicularis. On each side of this lamina there is a large foramen through which the olfactory nerves pass to the nasal capsules. Each nasal sac rests upon a broad subnasal lamina, and is separated from its fellow by the internasal prolongation of the lamina perpendicularis, which finally terminates in a short conical prenasal process. The capsules are not invested by even the rudiments of alinasal outgrowths.

The occipital plane is greatly inclined forwards. The large basioccipital bone (*bo*) probably represents, in addition to its own proper element, the centra of at least two of the most anterior vertebræ; that this is so is probable from the fact that two neural arches are attached to the hinder part of the bone. Two large exoccipitals (*ex.o*) uniting below with the basioccipital by a persistent suture, and separated from each other superiorly by a narrow interspace of cartilage, bound the foramen magnum. The outer margin of each bone is deeply cleft by the foramen (*Vg*) for the vagus nerve. There is no proper supraoccipital.

In the auditory capsule there are distinct epiotic, opisthotic, sphenotic, and prootic ossifications. The epiotics (*ep.o*) are small, triangular ossicles, occupying their normal position in

relation to the arch of the posterior vertical semicircular canal, and situated immediately over the exoccipitals.

The opisthotics (*op.o*) protect the postero-lateral angles of the cranium, and, in conjunction with the exoccipitals, bound the vagus foramen. A small projecting spur unites the opisthotic to the prootic. The prootic (*pr.o*) is the largest of the otic bones. Externally it is nearly circular in shape, but is deeply notched in front for the exit of the facial nerve, and behind it gives up a process which suturally unites with the spur from the opisthotic. Though the prootics do not develope the descending outgrowths so characteristic of Teleostei, yet they give off internal plates which, uniting with each other in the median line of the cranial floor, form a characteristic 'prootic bridge' (Fig. 5).

The sphenotic bones (post-frontals) (*pt.f*) occupy the antero-lateral angles of the otic capsules.

There is no pterotic bone. As in Polypterus the pterotic region of the auditory capsule is covered by the lateral margin of the parietal.

With the single exception of the prootics none of the otic bones are visible from the inside of the cranial cavity; and, with the exception of the slender connection of the opisthotic and prootic elements, the otic bones are separated from one another by wide interspaces of cartilage. The prootic alone is traversed by the particular semicircular canal with which it is in relation; the remaining otic bones lie entirely superficial to their respective canals which traverse the cartilage only.

In front of the lateral alæ of the parasphenoid, and between the foramina for the fifth and optic nerves, is the alisphenoid (*al.s*). This bone is almost circular in shape; from the middle of its outer surface a small spicule of bone is given off, which arches over the canal for the orbital muscles and abuts against the smaller of the two lateral processes of the parasphenoid.

This descending process bears a singular resemblance to the "descending process of the alisphenoid" so common among Mammalia. The alisphenoid is perforated by a foramen for the first division of the fifth nerve (*V′*), and a little below this

aperture there is a second foramen for the exit of the second and third divisions of the same nerve (*V″* and *V‴*).

The orbitosphenoids (*o.s.*) resemble the alisphenoids in size and in their nearly circular outline; they are thin above and support the descending cartilaginous "roof-plates," but are much thicker below, where they rest upon the thickened lateral edges of the coalesced trabeculæ. Viewed from the interior of the cranium their inferior edges are seen to approach closely to each other, though they remain separated by the cartilage which forms the floor of the trabecular groove. The hinder border of the bone is suturally connected with the alisphenoid, and is cleft nearly to its centre by a triangular fissure for the passage of the optic nerve (II). An examination of the interior of this part of the cranial cavity shows that the wide and shallow pituitary fossa is bounded behind by the "prootic bridge" (*Pro.*), beneath which the fossa is prolonged for some distance, while the anterior clinoid wall is cartilaginous. A strong fibrous membrane forms a floor to the fossa, and in addition extends between the alisphenoids and orbitosphenoids and the subjacent cartilage, surrounding the optic nerves, and filling up what would otherwise be a considerable vacuity in the cranial walls. Immediately in front of the fossa the cartilage of the cranial floor is perforated by two small foramina for the entrance of the carotid arteries.

Resting upon, and in part embedded in, the cartilaginous anterior clinoid wall there are two small osseous nodules (*b.s.*). Each ossicle is triangular in shape, with its broad end resting on the cartilage, from the ossification of which the bone is, apparently, in part formed, while the apex extends into the fibrous membrane which has been described as forming the floor of the pituitary fossa. From the position of these ossicles it is probable that ossification commenced in the fibrous membrane, and that subsequently it invaded the anterior clinoid wall. Although these ossicles have only a fibrous connection with the alisphenoids their position and relations point to their homology with the prepituitary portion of the basisphenoid of other Fishes. According to Mr Parker[1] the

[1] Development of the Salmon's skull, *Phil. Trans.*, 1872.

prepituitary element of the basisphenoid in the Salmon first appears as an ossification in the membranous septum behind the optic nerves. At first this ossification is quite distinct from the adjacent cartilage, but as ossification advances the cartilage is invaded and the exosteal rudiment becomes a true endosteal centre. Thus, from their position in relation to the "trabecular crest," and in their in part membranous origin, these ossicles in Amia agree with the basisphenoid of the young Salmon. The existence of paired ossicles is no objection to the homology suggested, as in the Ophidia the basisphenoid has a similarly double origin. If these ossicles are rightly determined as representing a basisphenoid, then Amia differs from all other living Ganoids, and agrees with the Teleostei in possessing a rudiment of that bone.

I may add, that a careful examination of a fresh skull of Lepidosteus failed to reveal the existence of similar structures in that ganoid. In Lepidosteus the cartilage which forms the anterior clinoid wall is produced upwards on each side between the foramina for the fifth and optic nerves, till it reaches the lower edge of the alisphenoids; but there are no ossifications either in the cartilage itself or in the fibrous floor of the fossa. In this fish, as in Amia, the posterior clinoid wall is formed by a "prootic bridge."

The conjoined trabeculæ which together form the cartilaginous basis cranii are continued forwards from the basioccipital as a flat band-like tract forming a floor to the interorbital extension of the cranial cavity. A shallow, longitudinal and median groove, in which the upwardly projecting keel of the parasphenoid lies, extends along this area, and evidently marks the line of coalescence of the trabeculæ. The cartilage forming the bottom of the groove is more transparent than the thicker lateral edges, and hence the primitive distinctness of the trabeculæ is well indicated.

Between the nasal capsules the basis cranii widens out into a quadrangular area formed largely by the subnasal lamina. The postero-lateral angles of this area are occupied by the prefrontals, and the antero-lateral angles by the two bones to be presently described.

The prefrontals (*pr.f*) are separated from the orbito-

sphenoids by a wide tract of cartilage. Internally they bound the foramen for the orbito-nasal nerve, and inferiorly each has a deeply grooved articular surface for the palatine bone. The prefrontals are overlaid by small but distinct ganoid plates (Fig. 1), which appear as the outer and anterior corners of the frontal bones.

The lamina perpendicularis is quite unossified, hence there is no true ethmoid as there is in Polypterus.

The two ossifications above referred to as forming the antero-lateral angles of the internasal area are peculiar to Amia amongst Ganoids. They lie, one on each side of the base of the prenasal process, and appear to be ossifications in the cartilage of the floors of the nasal capsules; inferiorly they rest on the upper surfaces of the vomers.

There can, I think, be but little doubt that these ossicles (*sep.mx*) are homologous with the paired endosteal ossifications, which are to be found at the distal end of the great prenasal rostrum in the Pike. In fact, if the prenasal region in Amia were produced anteriorly into a rostrum comparable to that of the Pike, these bones would exactly resemble in position and relations their homologues in the latter fish. These ossicles would also appear to be homologous with the septo-maxillary bone described by Mr Parker as existing in the floor of the nasal capsules in the Frog; and also with similar bones in the Ophidia. A section carried through these bones and the adjacent cartilage in Amia would resemble in all essentials the various sections given in Mr Parker's paper[1] on the development of the Frog's skull (Pl. x.).

Palato-pterygoid apparatus and suspensorium. (Fig. 6.)

The palato-pterygoid apparatus is constructed on the normal Teleostean type as regards the number and mutual relations of its component bones. It consists of a thin axial core of cartilage which posteriorly becomes continuous with a projecting spur of the quadrate, and anteriorly, in the prefrontal region, swells out into a thickened mass of cartilage and bone overlying the exosteal portion of the palatine. In connection with this

[1] *Phil. Trans.*, 1871.

axial core, palatine, pterygoid and mesopterygoid elements are developed.

The palatine (*pa*) is well developed, greatly exceeding in size its homologue in Polypterus; it is composed of two distinct elements, an exosteal lamina which forms the inferior part and lateral margin of the bone, and an endosteal portion by which the anterior part of the arcade is connected with the prefrontal, and apparently formed by the ossification of a mass of cartilage similar to that which in the Salmon performs a like function. The exosteal element is prolonged forwards in front of the prefrontal bone so as to be ultimately connected with the premaxilla, vomer, and septo-maxillary. It carries two kinds of teeth—long curved teeth arranged along its lateral margin, and resembling those in the premaxillæ, with which they form a continuous series; and a group of short obtusely conical teeth situated internally to those last mentioned, and continuing the series of vomerine teeth.

The endosteal portion of the palatine is triangular in shape, and cancellous in structure. Its superior surface, together with the adjacent cartilage, form an antero-posterior groove for the articulation of the arcade with the prefrontal. The prolongation of the palatine in front of its prefrontal articulation is a well-marked Teleostean modification possessed, so far as is known, by no other living Ganoid.

Behind the palatine the axial cartilage is invested on its inner side by a mesopterygoid (*m.pg*). This bone affords a floor to the orbit. In shape it is triangular, with the apex directed forwards, and overlapping the inner surface of the palatine; its posterior edge is adherent to the inner surface of the metapterygoid, while its superior margin almost touches the outer edge of the parasphenoid. The inner surface of the mesopterygoid is garnished with a number of very small teeth. The pterygoid is an elongated slender bone, which, by means of a small outer and a larger inner plate, clamps the lower edge of the cartilage. Anteriorly this bone unites suturally with the palatine; behind it is applied to the inner side of the distal end of the quadrate, while the outer plate overlaps the inferior two-thirds of the metapterygoid. On the palatine end of the bone there are a few teeth. The tripartite metapterygoid (*mt.pg*) is of

unusual size, and in shape is not unlike that of the Salmon, but instead of lying, as in that fish, immediately over the quadrate, it is situated almost entirely in front of that bone. The small process, which is just indicated in the Salmon, becomes in Amia a conspicuous cartilage-tipped process, rising from the middle of the curved upper surface of the bone, and reaching almost to the level of the cranial end of the hyomandibular. This process seems to represent either the orbitar process of the mandibular arch, or the summit of the arch. The pointed anterior end of the bone almost touches the descending process of the alisphenoid; the straight hinder edge is applied to the inner side of the quadrate, reaching nearly to the articular end of that bone[1]. The quadrate has the usual triangular shape. The hinder margin is grooved for the symplectic, and the apex carries a rounded condylar facet for articulation with the mandible. The front edge of the bone is produced into a forwardly projecting process, with which the axial cartilage of the palatopterygoid arcade becomes continuous.

The hyomandibular (*h.m*) does not articulate with any of the otic bones, but is applied to a groove in the cartilage of the otic region immediately over the prootic and opisthotic bones. The posterior border has a strong knob for the operculum, and its middle is obliquely perforated by a foramen for the facial nerve. The wide synchondrosis which unites the hyomandibular and symplectic bones has a well-marked backwardly projecting "knee," and is grooved by an articular surface for the cartilaginous interhyal. The symplectic (*sym*) is rather large, and is firmly attached, but not anchylosed, to the quadrate. Its cup-shaped distal end furnishes an articular surface for one of the ossicles in the adjacent end of the mandible.

The long axis of the hyomandibular is directed backwards and downwards, and is almost at right angles to the axis of the symplectic, which is directed forwards. It is possible that this angulation of the proximal half of the second postoral arch may account for the forward position of the metapterygoid.

[1] The tripartite shape of the metapterygoid suggests that possibly its three divisions may correspond to the 'pedicle', 'ascending process', and 'otic process' of the Amphibian suspensorium, but the condition of my specimen was such that I could not ascertain the relations of these processes to the branches of the fifth nerve.

The Mandible. (Fig. 7.)

The mandible is an unusually complex structure, as each ramus consists of not fewer than fourteen distinct elements. Meckel's cartilage persists as a thin axial band of cartilage. Its distal end is ossified, and forms a small cylindrical mento-meckelian ossicle (*mt.mk*), which lies in a groove on the inner side of the symphysial end of the dentary (*d*). The proximal end of the cartilage is the seat of at least four distinct ossific centres. Of these, three are arranged in a linear series proceeding from the angular extremity of the mandible. These are referred to in the annexed plates as *a*, *b*, and *c*. Of these the ossicles *a* and *b* form the anterior and posterior boundaries of the articular cup for the quadrate, and are separated from each other by that portion of Meckel's cartilage which forms the bottom of the cup. The bone marked '*c*' is much smaller than the other two. That part of Meckel's cartilage adjacent to the articular cup is produced vertically upwards and forwards into a well-marked "coronoid process" (*cr*). The base of this process is the seat of an ossification (*d*) which forms the outer side of the articular cup, and fits into the cup-shaped distal end of the preoperculum. Thus these three bones, *a*, *b*, and *c*, contribute to the formation of the concave articular surface for the quadrate.

Hitherto it has been currently stated in anatomical text-books that the mento-meckelian bone at the distal end, and the articular bone at the proximal end of Meckel's cartilage, were the only elements of the mandible really formed by ossification of the cartilage itself; yet in Amia there can, I think, be but little doubt that at least four, and probably five, ossific centres are developed in the axial cartilage.

Whether one of the centres *a*, *b*, *c*, and *d* represent the os articulare of the Teleostean mandible, or whether the latter bone is really a compound bone resulting from the coalescence of the persistently distinct elements of Amia, is not very evident; but I am inclined to think that the os articulare is not so simple a bone as it has hitherto been supposed to be.

As the Meckelian cartilage is the distal, or ventral half of the first postoral visceral arch, though it may not be possible to point out the special homologies of the mento-meckelian,

and the ossicles *a*, *b*, *c*, and *d*, with the ossifications found in the ventral halves of the remaining postoral arches, yet I think that we may roughly correlate those ossicles with the interhyal, epihyal, ceratohyal and hypohyal of the hyoidean series.

It may also be that the cartilaginous "coronoid process" is another instance of the tendency manifested by the first postoral arch to develope forward connective outgrowths, of which the orbitar process and the palato-pterygoid arcade are conspicuous examples in the proximal half of this arch.

In addition to the mandibular elements above referred to there are, in addition, several membrane bones. The ossification '*a*' has a small ganoid plate (*d.a*) attached to it, which appears at the extreme tip of angle of the jaw. Just behind this there is a large angular element (*Ag*), and above this splint and applied to the outer surface of the coronoid cartilage there is a supra-angular piece (*s.ag*). The dentary (*d*), shaped like a half cylinder, completes the series of splints seen on the outer side of the ramus. The inner side of the Meckelian cartilage is invested by a large triangular splenial[1] piece, and, as in Polypterus and Ceratodus among Ganoids, and in Siren and larval Salamanders among Amphibia, carries a number of small teeth. Amia also further resembles the young Polypterus, in that the splenial does not extend continuously to the symphysis, but the interval is occupied by a series of five small thin teeth-bearing plates. The splenial teeth, and those carried by the last mentioned ossicles form a continuous series parallel to the much larger, curved teeth carried by the dentary. There is no coronary splint.

Hyoidean and branchial arches.

These structures scarcely, if at all, differ from those of the ordinary Teleostean. The inter-hyal is a small square piece of cartilage attached to a groove in the cartilaginous interspace between the hyomandibular and symplectic. The epihyal has a rounded condyle for articulation with a cup in the adjacent extremity of the interhyal. A ceratohyal and a hypohyal complete the arch.

[1] The splenial element is not shewn in the figures.

There are five branchial arches, and of these the first four are complete, containing pharyngo-branchial, epi-branchial, cerato-branchial and hypo-branchial elements; the fifth arch has the cerato-branchial only represented by bone. The hypo-branchial of the third and fourth arches are bifurcate at the ventral ends. The epihyal of each arch gives off a short, backwardly projecting process which is attached to the pharyngo-branchial of the arch behind it. The basi-branchial elements, four in number, are laterally compressed pieces of bone and cartilage, and only one of them is ossified.

Cranial distribution of the Mucous Canals.

The main lateral canal of each side penetrates the post-temporal, supra-temporal, 'parietal' and nasal bones, and then, instead of joining the transverse ethmoidal branch, as might have been expected, it appears to terminate in three short branches opening at the surface between the nasals, the ethmoid and the præ-orbital bones. Commissural and other branches are given off from each lateral trunk. A transverse canal, traversing the two supra-temporals, connects the lateral canals of opposite sides. A mandibular branch (*s.lc*) leaves each lateral canal in the parietal, and passing downwards through the pre-operculum, as in Teleostei, pierces the angular element, and traverses the dentary to effect a junction with its fellow of the opposite side. Finally, a suborbital branch leaves the lateral canal in the vicinity of the dermo-sphenotic and, perforating that bone, passes downwards and forwards through each of the post-orbital bones, through the suborbital, lachrymal and præ-orbital bones, to the transverse part of the dermo-ethmoid where it joins the corresponding division of the other side.

Numerous pores connect all these canals with the surface at irregular intervals.

Summary.

In summarising the results of the foregoing description of the skull of Amia, I would lay stress on the following facts, as having a special bearing on the affinities of Amia to the more highly specialized osseous fishes and to the Amphibia.

I. The possession of a complete chondrocranium, *i.e.* the absence of fenestræ in the cranial roof, as in Lepidosteus, and the Pike (Esox).

II. The existence of a nearly complete series of otic bones, comprising a large prootic with internal plates forming a characteristic "prootic bridge" in the floor of the cranium, opisthotic, epiotic, and sphenotic elements.

III. The presence of two ossific centres, partly exosteal and in part endosteal, forming rudimentary basi-sphenoid.

IV. Septo-maxillary ossifications in the subnasal lamina, as in Clarias, Esox, Rana and Ophidia.

V. The interorbital prolongation of the cranial cavity, separating distinct, paired ali- and orbito-sphenoids.

VI. The prolongation of the palatine in front of its prefrontal articulation and the connection of its anterior end with the inwardly curved process of the maxilla.

VII. The possession of a T-shaped dermal ethmoid overlying the premaxillæ, and the close analogy in number and relations between the investing ganoid plates of Amia and those of the Siluroidei, and especially with those of Clarias, as has been previously described.

VIII. A complete series of opercular bones, a preoperculum anchylosed to the hyomandibular and symplectic bones, an operculum, or interoperculum, and a suboperculum.

IX. The presence of a jugal bone attached as in Teleostei to the upper edge of the posterior part of the maxilla.

X. The existence of a mento-meckelian ossicle, as in Spatularia, and of several additional centres of ossification in the proximal extremity of Meckel's cartilage.

XI. The presence of five accessory dentigerous splenial elements in addition to the normal mandibular splints, as in the young Polypterus and Ceratodus among Ganoids, and in Siren and larval Salamanders among Amphibia.

In combining in its cranial structure the anatomical facts expressed in paragraphs I—IX inclusive, Amia differs from all other living Ganoidei, and exhibits distinct and decided affinities to such generalized types of physostomous Teleostei as the Siluroidei, Cyprinoidei, &c. On the other hand, in common with all other Ganoids, Amia possesses several points of resemblance with larval and adult forms of Amphibia, especially as regards the structures to which attention has been directed in paragraphs IV, X, and XI. Moreover, in the angulation of the mandibular arch caused by the forward growth of its metapterygoid element, we have a repetition of an arrangement characteristic of the adult Frog, and of certain Selachians (Notidanus). But, notwithstanding these evidences of widespread affinity, it is evident that if, in addition to the above-mentioned facts, we accredit Amia with the possession of cycloid scales, non-lobate fins, a nearly homocereal tail, and note the absence of spiracles, the Teleostean affinities predominate; and it may be asked whether, despite certain peculiarities in the structure of its generative organs and bulbus arteriosus, the gap between the ganoid Amia and the physostomous Teleostei is not less than need be expressed by ordinal distinction.

It may be that just as Polypterus and its near ally of the same family are the sole surviving examples of the otherwise long extinct order of Crossopterygian Ganoids, so the Amiidæ are the sole survivors of those widely generalized Ganoidei, out of which more specialized Teleostei were directly evolved.

EXPLANATION OF PLATES.

For the drawings from which the accompanying plates were taken, I am indebted to Mr J. W. Clark, whose kindness I gratefully acknowledge. Figures VI. and VII. were drawn for me by Mr C. H. Haddon, of Christ's College. The figures are all of life-size, and the lettering is uniform throughout.

al. s.	alisphenoid.
ag.	angular.
bo.	basioccipital.
b. s.	basisphenoid.
cr.	coronary cartilage.
ct.	cerato-hyal.
d. ptf.	dermo-postfrontal.
d. so.	dermo-supraoccipital.
d.	dentary.
da.	dermal part of 'a.'
eth.	ethmoid.
ep. o.	epiotic.
eph.	epihyal.
ex. o.	exoccipital.
fr.	frontal.
h. m.	hyomandibular.
i. op.	interoperculum.
jg.	jugal.
l.	lachrymal.
Mk.	Meckel's cartilage.
mt. mk.	mento-meckelian.
mx.	maxilla.
m. pg.	mesopterygoid.
mt. pg.	metapterygoid.
a., *b.*, *c.*, *d.*	ossifications in Meckel's cartilage
n.	nasal.
nl. a'., *nl. a''.*	neural arches attached to basi-occipital.
os.	orbitosphenoid.
op. o.	opisthotic.
op.	operculum.
pa.	parietal.
pr. o.	prootic.
pt. f.	postfrontal (sphenotic).
pr. f.	prefrontal.
p. op.	preoperculum.
pt. orb.	postorbital.
p. mx.	premaxilla.
p.n.	prenasal process.
pa. s.	parasphenoid.
p. tp.	post-temporal.
pr. orb.	preorbital.
pg.	pterygoid.
q.	quadrate.
s. orb.	suborbital.
sp. mx.	septo-maxillary bone.
s. op.	suboperculum.
s. tp.	supra-temporal.
s. ag.	supraangular.
sym.	symplectic.
vo.	vomer.
II.	Foramen for optic nerve.
V'.	" for first division of the fifth nerve.
V''., V'''.	" for second and third divisions of the fifth nerve.
VII.	" facial nerve.

Fig. I. Upper surface of the cranium of Amia with the ganoid plates *in situ*.

Fig. II. Lateral view of the same.

Fig. III. Skull of Amia seen from below. The parasphenoid and vomer are seen, and in addition, the inner side of the palatopterygoid arch; this arch has been removed on the right side.

Fig. IV. Lateral view of the cranium, with the ganoid plates and palatopterygoid apparatus removed.

Fig. V. View of interior of cranial cavity; the ganoid plates and part of the cartilaginous cranial roof have been removed so as to show the basisphenoid and the "prootic bridge."

Fig. VI. Palatopterygoid arcade, with hyomandibular, metapterygoid, quadrate and preoperculum attached.

Fig. VII. Inner side of the mandible: the splenial has been removed in order to show Meckel's cartilage and its accessory ossifications.

EXPERIMENTS ON THE BILIARY SECRETION OF THE DOG. By Prof. RUTHERFORD and M. VIGNAL.

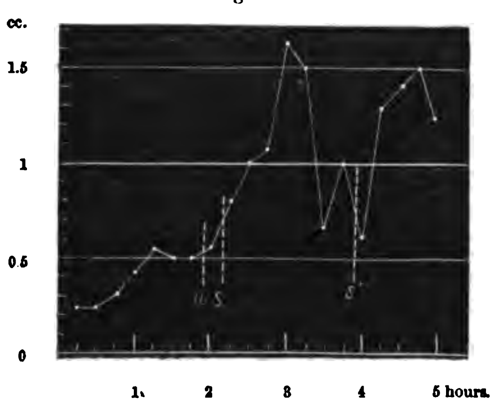
Third Series[1].

ACTION OF SODIUM SULPHATE.

WORKS on Therapeutics generally make no mention of any cholagogue action of this substance. In the fourth edition of Garrod's *Materia Medica,* however, it is stated, that in addition to its action as a saline purgative it "probably influences the biliary secretion."

Experiment 1. Dog that had fasted 19 hours. Weight 19.5 kilogrammes. (Fig. 1.)

Fig. 1.



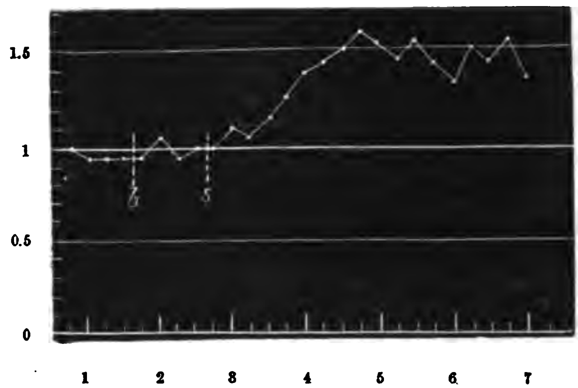
Secretion of bile before and after sodium sulphate. 21 cc. water injected into duodenum at *w*. 60 grains sodium sulphate in 12 cc. water injected at *s*, and again at *s'*.

AUTOPSY. Evidence of decided purgative action in small intestine, the mucous membrane of which exhibited a considerably increased vascularity.

[1] The First Series appeared in this *Journal* Vol. x. p. 253, the Second Series in the present Vol. p. 61.

Experiment 2. Dog that had fasted 20 hours. Weight 15.7 kilogrammes. (Fig. 2.)

Fig. 2.



Secretion of bile before and after sodium sulphate. 3 cc. bile and 5 cc. water—heated to 37°C.—injected into duodenum at *b*. 508 grains sodium sulphate—in the same fluid heated to 37°C., injected at *s*.

AUTOPSY. Mucous membrane of whole length of small intestine slightly reddened. The small intestine contained 147 cc. of clear fluid with greenish flakes; thus affording evidence of a decided purgative effect.

Results of Experiments with Sodium Sulphate.—Doses of 60 grains twice repeated (Experiment 1), and a single dose of 508 grains (Experiment 2), increased the biliary secretion. Sodium sulphate is undoubtedly, therefore, a hepatic stimulant, but not of great power, for even in the second case the secretion of bile per kilogramme of body-weight did not rise higher than 0.388 cc. per hour. The positive character of this result is important, because it is well known that the waters of Carlsbad have a cholagogue action, and although they contain in addition to sodium sulphate, sodium carbonate, sodium chloride, potassium sulphate, and small quantities of other substances, sodium sulphate is the principal salt, and to it the cholagogue action is doubtless chiefly due.

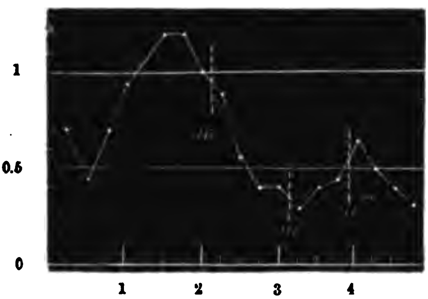
Sodium sulphate, however, has for a considerable time been—in practical medicine—almost entirely superseded by magnesium sulphate, on account of its "more agreeable taste"

(Garrod): we therefore performed the two following experiments to determine whether or not this substance is a cholagogue.

ACTION OF MAGNESIUM SULPHATE.

Experiment 3. Dog that had fasted 17 hours. Weight 5.4 kilogrammes. (Fig. 3.)

Fig. 3.

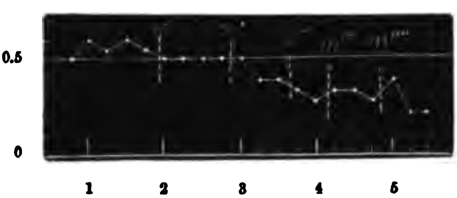


Secretion of bile before and after magnesium sulphate. 60 grains in 6 cc. water injected into duodenum at *m*, *m'* and *m''* (180 grains given in all).

AUTOPSY. Great purgative action in upper half of small intestine. Mucous membrane intensely reddened.

Experiment 4. Dog that had fasted 17 hours. Weight 8.2 kilogrammes. (Fig. 4.)

Fig. 4.



Secretion of bile before and after magnesium sulphate. 60 grains in 12 cc. water at *m*. 60 grains in 6 cc. water at *m'*, *m''*, *m'''*, and 120 grains in 12 cc. water at *m''''*, all injected into duodenum (360 grains given in all).

AUTOPSY. Small intestine contained 90 cc. of fluid, whereas only 42 cc. had been injected. There was, therefore, evidence of decided purgation, and there was intense irritation of the mucous membrane in the upper half of the small intestine.

Results of Experiments with Magnesium Sulphate.—Experiment 3—but especially experiment 4—clearly show that, unlike sulphate of soda, magnesium sulphate has no cholagogue action. The curve in experiment 4 exhibits remarkably well the effect on the secretion of bile, produced by a substance that stimulates the intestinal glands, but not the liver. *In such a case the biliary secretion is simply diminished.*

Experiment 1.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.25	
	0.25	
	0.30	
	0.40	
	0.55	
	0.50	
	0.50	0.107 cc.
w	—	
	0.55	
s	—	
	0.80	
	1.00	
	1.05	0.266 cc.
	1.65	
	1.50	
	0.65	
	1.00	
s′	—	
	0.60	
	1.30	
	1.40	0.279 cc.
	1.50	
	1.25	

Experiment 2.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.00	
	0.95	
	0.95	
	0.95	
b	—	
	0.95	
	1.05	0.251 cc.
	0.95	
	1.00	
s	—	
	1.00	
	1.10	
	1.05	
	1.15	
	1.25	
	1.40	
	1.45	
	1.50	
	1.60	0.388 cc.
	1.55	
	1.45	
	1.55	
	1.45	
	1.35	
	1.50	
	1.45	
	1.55	
	1.35	

Experiment 3.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.70	
	0.45	
	0.70	0.564 cc.
	0.95	
	0.95	
	1.20	
	1.20	
	1.00	
m	—	
	0.90	
	0.55	
	0.40	
	0.40	
m′	—	
	0.30	
	0.40	
	0.45	
m″	—	
	0.65	
	0.50	0.342 cc.
	0.40	
	0.30	

Action of Potassium Sulphate.

Potassium sulphate is sometimes employed as a purgative agent, but no mention is made in the books, of its having any action on the liver. Dr Wade of Birmingham, however, informed us that he finds this substance a cholagogue in man,

and at his request we tested by our method its action on the liver of the dog.

Experiment 4.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.50	
	0.60	
	0.55	0.28 cc.
	0.60	
	0.55	
m	—	
	0.50	
	0.50	
	0.50	
	0.50	
m′	—	
	0.50	
	0.40	
	0.40	
m″	—	
	0.35	
	0.30	
m‴	—	
	0.35	
	0.35	
	0.30	
m″″	—	
	0.40	0.146 cc.
	0.25	
	0.25	

Experiment 5.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.45	
	1.40	
	1.35	
	1.40	
	1.32	
b	—	
	1.32	
	1.32	0.315 cc.
	1.40	
	1.32	
p	—	
	1.40	
	1.32	
	1.40	
	1.42	
	1.20	
	1.52	
	1.42	
	1.35	
	1.40	
	1.42	
	1.35	
	1.42	
	1.20	
	1.35	
	1.20	
	1.45	
	1.27	
	1.27	
	1.17	
	1.22	0.266 cc.
	1.10	
	1.02	

Experiment 7.

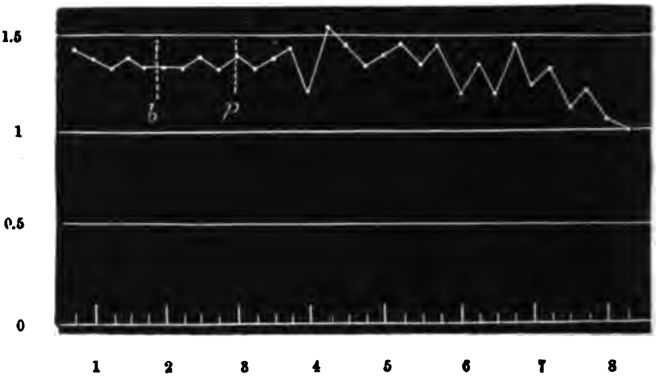
	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.80	
	1.90	
	1.70	
	1.65	0.316 cc.
	1.65	
	1.70	
p	—	
	1.80	
	1.70	
	1.90	
	1.80	
	1.90	
	2.05	
	2.07	
	2.10	
	2.25	
	2.37	
	2.45	
	2.40	
	2.45	
	2.50	
	2.47	
	2.55	
	2.55	
	2.57	0.47 cc.
	2.45	
	2.40	
	2.30	
	2.40	
	2.40	
	2.20	
	1.95	0.352 cc.
	1.20	

Experiment 5. Dog that had fasted 17 hours. Weight 17 kilogrammes. (Fig. 5.)

AUTOPSY. Small intestine contained 137 cc. greenish fluid with mucous flakes. The mucous membrane exhibited increased vascularity with small ecchymoses in its upper fourth.

In this case, therefore, this substance irritated the intestine and produced purgation, but did not excite the liver. It was decided to give in the next case a larger dose.

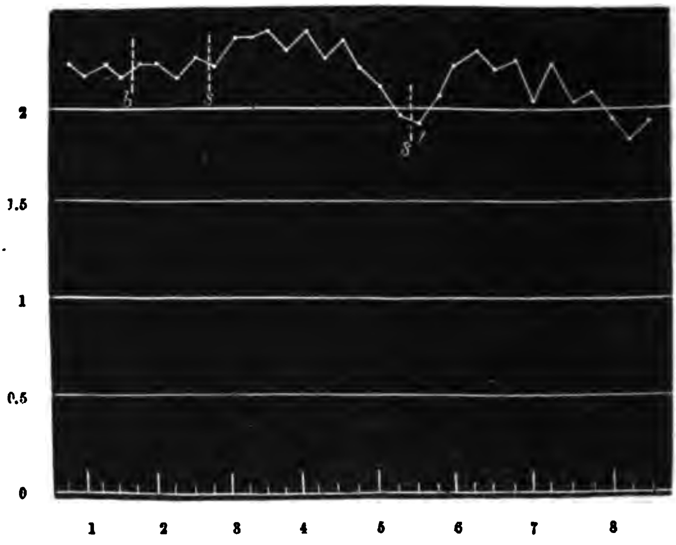
Fig. 5.



Secretion of bile before and after potassium sulphate. 2½ cc. bile and 16 cc. water injected into duodenum at *b*. The same with 124 grains potassium sulphate heated to 37°C. injected at *p*.

Experiment 6. Large dog that had fasted 17 hours. Its weight unfortunately was not recorded. (Fig. 6.)

Fig. 6.



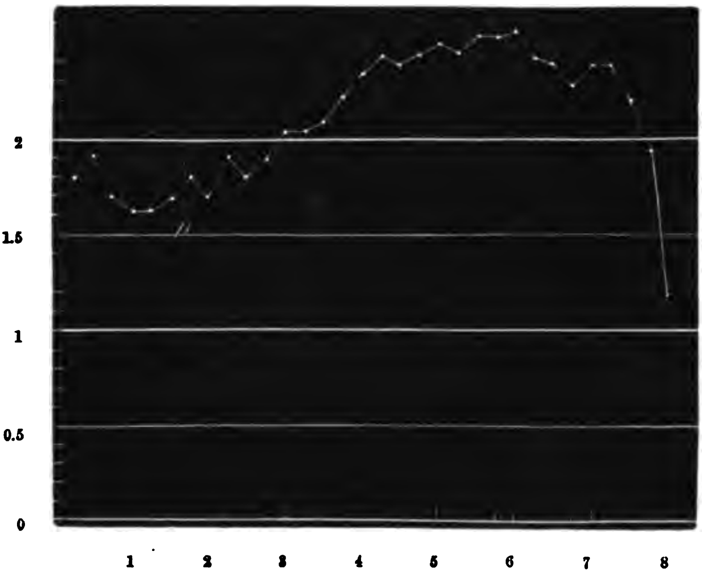
Secretion of bile before and after potassium sulphate. 2½ cc. bile and 35 cc. water injected into duodenum at *b*, the same with 142 grains potass. sulph. injected at *s* and again at *s'*.

AUTOPSY. Small intestine contained 143 cc. watery fluid. The vascularity of the mucous membrane in the whole length of the small intestine was slightly increased.

There being in this case evidence of a slight increase of the biliary secretion, another experiment was thought desirable.

Experiment 7. Dog that had fasted 17 hours. Weight 21.5 kilogrammes. (Fig. 7.)

Fig. 7.



Secretion of bile before and after 232 grains potassium sulphate dissolved in 82 cc. water at 37°C. and injected into duodenum at *p*.

AUTOPSY. Increased vascularity of mucous membrane in whole length of small intestine. The small intestine contained 90 cc. clear brownish fluid with numerous mucous flakes. There was, therefore, evidence of considerable purgative action.

Results of Experiments with Potassium Sulphate.—Experiment 7 clearly shows that potassium sulphate is undoubtedly a hepatic stimulant. The dose of 232 grains, given in this case to a full-sized dog, was just the maximum dose for a man. The negative effect of 124 grains in experiment 5, and the slight effect of 142 grains twice repeated in experiment 6,

suggest that this substance is uncertain in its action on the liver. Regarding its action on the intestinal glands, however, there was no uncertainty, for its purgative effect was pronounced in all the three experiments. Possibly the sparing solubility of the salt may render its absorption into the portal vein uncertain. The bile given along with the salt in experiments 5 and 6 had probably nothing whatever to do with the result. The result of experiment 7 completely supports Dr Wade's opinion, that potassium sulphate is a cholagogue. Indeed, the amount of bile secreted per kilogramme of body-weight under its influence in experiment 7 was greater than in either of the experiments with sodium sulphate (1 and 2). The apparent uncertainty, however, in the action of potassium sulphate must not be lost sight of.

Action of Sodium Phosphate.

Sodium phosphate is described in the text-books as a mild saline purgative; nothing being said about its action as a cholagogue. Professor Stephenson of Aberdeen, however, has found it specially useful for children when there is a deficiency of bile in the discharges (*Edinburgh Medical Journal*, 1867, Vol. XIII. p. 336). The dose as a purgative for a man is 120—480 grains.

Experiment 8. Dog that had fasted 20 hours. Weight 26.9 kilogrammes. (Fig. 8.)

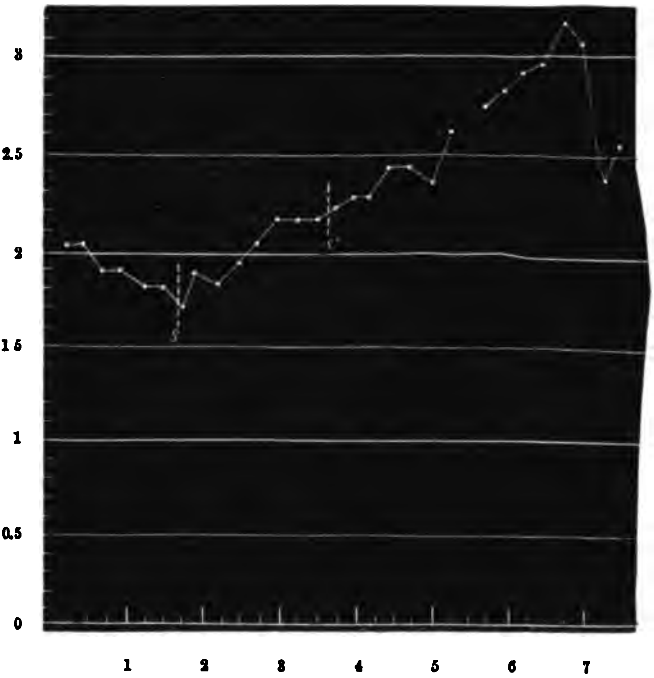
Autopsy. Somewhat increased vascularity of mucous membrane of small intestine. Evidence of a very decided purgative effect: the contents of the small intestine being of a very watery character.

Table I.

Composition of the Bile before and after Sodium Phosphate.

Experiment 8.	Before.	After.
Water	84.69	85.15
Bile-acids, pigments, cholesterin, fats	13.23	12.91
Mucus	1.01	0.93
Ash	1.07	1.01
	100.00	100.00
Velocity of secretion per half-hour	3.6 cc.	5.5 cc.

Fig. 8.



Secretion of bile before and after sodium phosphate. 77 grains in 15 cc. water injected into duodenum at *s*, and 124 grains in 25 cc. water injected at *s'*.

Results of Experiments with Sodium Phosphate.—1. This substance is undoubtedly a hepatic stimulant of very considerable power. 2. Although it renders the bile more watery, it increases the amount of biliary matter secreted per unit of time. 3. While acting as a purgative, it irritates the intestinal mucous membrane very slightly.

The results of experiment 8 were so satisfactory—both doses of the substance producing an effect—that it was thought needless to repeat it, as it confirms Dr Stephenson's observations on the human subject, adding to these, however, the definite knowledge that it has the power of actually increasing the flow of the bile, and that it does so by stimulating the hepatic cells.

Results of Experiments with Magnesium Sulphate.—Experiment 3—but especially experiment 4—clearly show that, unlike sulphate of soda, magnesium sulphate has no cholagogue action. The curve in experiment 4 exhibits remarkably well the effect on the secretion of bile, produced by a substance that stimulates the intestinal glands, but not the liver. *In such a case the biliary secretion is simply diminished.*

Experiment 1.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.25	
	0.25	
	0.30	
	0.40	
	0.55	
	0.50	
	0.50	0.107 cc.
w	—	
	0.55	
s	—	
	0.80	
	1.00	
	1.05	0.266 cc.
	1.65	
	1.50	
	0.65	
	1.00	
s′	—	
	0.60	
	1.30	
	1.40	0.279 cc.
	1.50	
	1.25	

Experiment 2.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.00	
	0.95	
	0.95	
	0.95	
b	—	
	0.95	
	1.05	0.251 cc.
	0.95	
	1.00	
s	—	
	1.00	
	1.10	
	1.05	
	1.15	
	1.25	
	1.40	
	1.45	
	1.50	
	1.60	0.388 cc.
	1.55	
	1.45	
	1.55	
	1.45	
	1.35	
	1.50	
	1.45	
	1.55	
	1.35	

Experiment 3.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.70	
	0.45	
	0.70	0.564 cc.
	0.95	
	0.95	
	1.20	
	1.20	
	1.00	
m	—	
	0.90	
	0.55	
	0.40	
	0.40	
m′	—	
	0.30	
	0.40	
	0.45	
m″	—	
	0.65	
	0.50	
	0.40	0.342 cc.
	0.30	

Action of Potassium Sulphate.

Potassium sulphate is sometimes employed as a purgative agent, but no mention is made in the books, of its having any action on the liver. Dr Wade of Birmingham, however, informed us that he finds this substance a cholagogue in man,

and at his request we tested by our method its action on the liver of the dog.

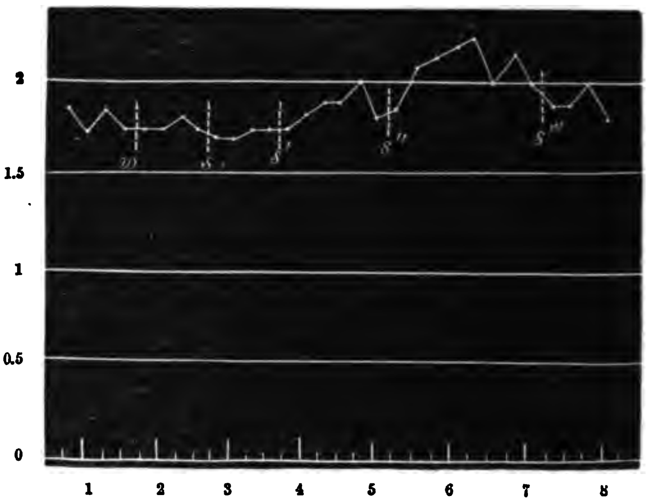
Experiment 4.		Experiment 5.		Experiment 7.	
Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
cc.		cc.		cc.	
0.50		1.45		1.80	
0.60		1.40		1.90	
0.55		1.35		1.70	
0.60	0.28 cc.	1.40		1.65	
0.55		1.32		1.65	0.316 cc.
m ——		*b* ——		1.70	
0.50		1.32		*p* ——	
0.50		1.32		1.80	
0.50		1.40	0.315 cc.	1.70	
0.50		1.32		1.90	
m′ ——		*p* ——		1.80	
0.50		1.40		1.90	
0.40		1.32		2.05	
0.40		1.40		2.07	
m″ ——		1.42		2.10	
0.35		1.20		2.25	
0.30		1.52		2.37	
m‴ ——		1.42		2.45	
0.35		1.35		2.49	
0.35		1.40		2.45	
0.30		1.42		2.50	
m⁗ ——		1.35		2.47	
0.40	0.146 cc.	1.42		2.55	
0.25		1.20		2.55	
0.25		1.35		2.57	0.47 cc.
		1.20		2.45	
		1.45		2.40	
		1.27		2.30	
		1.27		2.40	
		1.17		2.40	
		1.22		2.20	
		1.10	0.266 cc.	1.95	0.352 cc.
		1.02		1.20	

Experiment 5. Dog that had fasted 17 hours. Weight 17 kilogrammes. (Fig. 5.)

AUTOPSY. Small intestine contained 137 cc. greenish fluid with mucous flakes. The mucous membrane exhibited increased vascularity with small ecchymoses in its upper fourth.

In this case, therefore, this substance irritated the intestine and produced purgation, but did not excite the liver. It was decided to give in the next case a larger dose.

Fig. 11.



Secretion of bile before and after sodium chloride. 10 cc. water injected into duodenum at *w*. The same with 120 grains sodium chloride injected at *s*, *s'*, *s''*, *s'''* (480 grains given in all).

injected, decided purgative action had taken place. The vascularity of the mucous membrane was slightly increased.

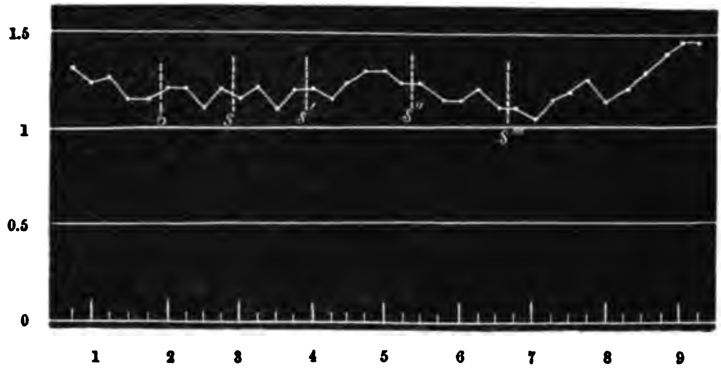
Result of Experiment with Sodium Chloride.—Inasmuch as the first three doses of sodium chloride, amounting in the aggregate to 360 grains, produced scarcely any effect on the secretion of bile, it may be concluded that this substance is a very feeble hepatic stimulant. Another experiment did not appear to be required.

Action of Sodium Bicarbonate.

Experiment 12. Dog that had fasted 18 hours. Weight 16.3 kilogrammes. (Fig. 12.)

Autopsy. The vascularity of the mucous membrane of the small intestine was slightly increased. The viscus contained 60 cc. of a greenish mucous fluid.

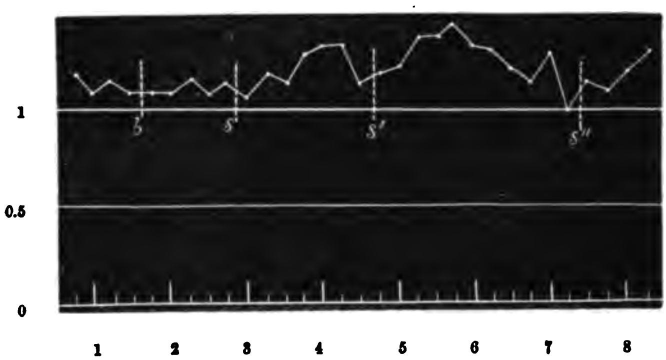
Fig. 12.



Secretion of bile before and after sodium bicarbonate. 5 cc. water and 2 cc. bile injected into duodenum at *b*. The same with 31 grains sodium bicarbonate injected at *s*, *s'* and *s''*. 15 cc. water with 2 cc. bile and 124 grains sodium bicarbonate injected at *s'''* (217 grains given in all).

Experiment 13. Dog that had fasted 18 hours. Weight 19.9 kilogrammes. (Fig. 13.)

Fig. 13.



Secretion of bile before and after sodium bicarbonate. 5 cc. water and 2.5 cc. bile injected into duodenum at *b*. The same with 64 grains sodium bicarbonate injected at *s*, *s'*, and *s''* (192 grains given in all).

Result of Experiments with Sodium Bicarbonate.—In experiment 12, the amount of bile secreted per kilogramme of body-weight during the first hour was 0.294 cc., during the seventh hour it was 0.287 cc.; and during the last hour—after 217

grains sodium bicarbonate had been given, it was 0.341 cc. In experiment 13 the secretion during the first hour was 0.23 cc. per kilogramme of body-weight; during the fifth hour, when the secretion was at its height, it was 0.28 cc. per kilogramme, 128 grains of sodium bicarbonate having been given. It is, therefore, evident, that this substance has scarcely any effect on the secretion of bile. Nevertheless, the slight effect perceptible in experiment 13 more especially, indicates an exciting influence on the liver, although an extremely feeble one.

Experiment 8.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	2.05	
	2.07	
	1.90	
	1.90	
	1.80	0.278 cc.
	1.80	
s	——	
	1.70	
	1.90	
	1.80	
	1.95	
	2.07	
	2.15	
	2.17	
	2.17	
s′	——	
	2.20	
	2.27	
	2.25	
	2.40	
	2.40	
	2.30	
	2.60	
	lost.	
	2.70	
	2.80	
	2.90	
	2.95	
	3.15	0.448 cc.
	3.05	
	2.30	
	2.57	

Experiment 9.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.25	
	0.15	
w	——	0.115 cc.
	0.15	
	0.05	
r	——	
	0.25	
	0.30	
	0.35	
r′	——	
	0.35	
	0.50	
	0.60	
r″	——	
	0.80	
	1.00	
r‴	——	0.653 cc.
	1.00	
	0.60	
	0.50	
	0.50	
	0.55	
	0.35	

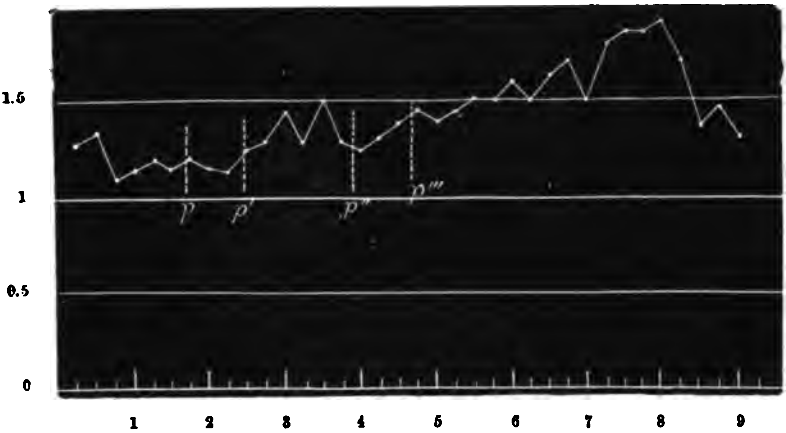
Experiment 10.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.75	
	0.70	
	0.70	
	0.70	
b	——	
	0.75	
	0.80	0.236 cc.
	0.70	
	0.70	
r	——	
	0.75	
	0.70	
	0.70	
	0.80	
	0.90	
	0.85	
	0.90	
	0.95	
	0.85	
	0.85	
	1.00	
	1.05	0.332 cc.
	1.00	
	1.10	
	1.00	
	0.90	
	1.00	
	0.90	
	0.70	

ACTION OF POTASSIUM BICARBONATE.

Experiment 14. Dog that had fasted 18 hours. Weight 19.3 kilogrammes. (Fig. 14.)

Fig. 14.



Secretion of bile before and after potassium bicarbonate. 31 grains in 8 cc. water injected into duodenum at *p*, *p'*, and *p''*. 108 grains in 8 cc. water injected at *p'''* (201 grains given in all).

AUTOPSY. 53 cc. of a clear brownish fluid, with numerous mucous flakes in small intestine. Vascularity of mucous membrane considerably increased.

Result of Experiment with Potassium Bicarbonate.—201 grains of this substance increased the secretion of bile but not to a great extent, for the bile-secretion per hour did not rise higher than 0·384 cc. per kilogramme of body-weight. Seeing that 31 grains produced no effect, it may be safely inferred that the dose of 10 or 15 grains often taken by a man does not appreciably affect his biliary secretion.

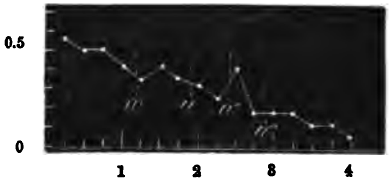
ACTION OF AMMONIUM CHLORIDE.

Chloride of ammonium is "by some considered a cholagogue" (Garrod's *Materia Medica*, 4th ed. p. 51). Dr W. Stewart (quoted in Wood's *Therapeutics*, 1874, p. 446) has recommend-

ed it in cases of chronic torpidity of the liver, to be given in doses of twenty grains thrice a day, for weeks or even months.

Experiment 15. Dog that had fasted 18 hours. Weight 7 kilogrammes. (Fig. 15.)

Fig. 15.

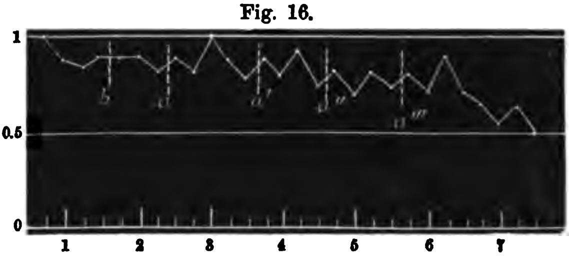


Secretion of bile before and after ammonium chloride. 6 cc. water injected into duodenum at *w*. The same with 6 grains ammonium chloride, injected at *a*, and again at *a′* and *a″* (18 grains given in all).

AUTOPSY. Small intestine, in nearly its whole length, contained a large quantity of a very watery fluid. The vascularity of the mucous membrane was only slightly increased.

Experiment 16. Dog that had fasted 20 hours. Weight 13.7 kilogrammes. (Fig. 16.)

Fig. 16.



Secretion of bile before and after ammonium chloride. ¼ cc. bile and 5 cc. water injected into duodenum at *b*. The same with 10 grains ammonium chloride injected at *a*. At *a′*, the same with 20 grains, at *a″* the same with 40 grains, at *a‴* the same with 60 grains.

AUTOPSY. Somewhat increased vascularity of the mucous membrane of the upper three-fourths of the small intestine. There was evidence of a moderate purgative effect.

Result of Experiments with Ammonium Chloride.—The two experiments with this substance show that doses capable of stimulating the intestinal glands did not excite the liver. The effect on the biliary secretion is comparable to that of

sulphate of magnesia (experiments 3 and 4), or other substance having a stimulant effect on Lieberkühn's glands, but not on the liver. Inasmuch, therefore, as these experiments give no evidence of any stimulant action of this substance on the liver, and seeing that in the human subject also there is no certain evidence of its having any *direct* cholagogue action, one is led to ask whether the effects observed by

Experiment 11.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.82	
	1.72	
	1.82	
	1.72	
w	—	
	1.72	
	1.75	0.28 cc.
	1.80	
	1.75	
s	—	
	1.70	
	1.70	
	1.75	
	1.75	
s′	—	
	1.75	
	1.85	
	1.90	0.306 cc.
	1.90	
	2.00	
	1.80	
s″	—	
	1.85	
	2.10	
	2.15	0.346 cc.
	2.20	
	2.22	
	2.00	
	2.15	
	2.00	
s‴	—	
	1.90	
	1.90	
	2.00	
	1.80	

Experiment 14.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.30	
	1.35	
	1.10	
	1.15	
	1.20	0.238 cc.
	1.15	
p	—	
	1.20	
	1.15	
	1.15	
p′	—	
	1.25	
	1.30	
	1.45	
	1.30	0.287 cc.
	1.50	
	1.30	
p″	—	
	1.25	
	1.30	
	1.40	
p‴	—	
	1.45	
	1.40	
	1.45	
	1.50	
	1.50	
	1.60	
	1.50	
	1.67	
	1.70	
	1.50	
	1.80	
	1.85	0.384 cc.
	1.85	
	1.90	
	1.70	
	1.40	
	1.45	
	1.30	

Experiment 16.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.00	
	0.90	0.267 cc.
	0.87	
	0.90	
b	—	
	0.90	
	0.90	
	0.85	
a	—	
	0.90	
	0.85	
	1.00	
	0.90	
	0.80	
a′	—	
	0.90	
	0.80	
	0.95	
	0.77	
a″	—	
	0.80	
	0.70	
	0.80	
	0.75	
a‴	—	
	0.80	
	0.70	
	0.90	
	0.70	
	0.65	
	0.55	0.169 cc.
	0.62	
	0.50	

Dr Stewart in cases of chronic hepatic torpidity, may not have been the result of some indirect action of the liver, due to a slight but prolonged increase of the intestinal secretion, or to some effect on the system generally.

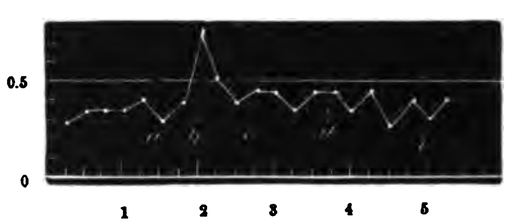
Action of Nitro-hydrochloric Acid.

The dilute nitro-hydrochloric acid employed by us was prepared thus (*British Pharmacopœïa*). Mix 3 cc. nitric acid with 4 cc. hydrochloric acid. After an interval of twenty-four hours, add 25 cc. water. The dose for a man is from 5 to 20 minims.

The employment of this substance in hepatic disorder was first recommended by Dr Scott of Bombay, who used it largely in "congestion of the liver." It was administered as a foot-bath, and also internally. Its effects, however, were by some held to be so doubtful, that its use appears to have been abandoned for a time (Christison's *Dispensatory*, 1848, p. 41). Annesley, Martin, and others—experienced in the diseases of India—have, however, supported the opinion held by Scott. Wood (*A Treatise on Therapeutics*, London, 1874, p. 88) maintains, from his own observation, that it increases the flow of the bile.

Experiment 17. A small dog (weight not ascertained) that had fasted 17 hours. (Fig. 17.)

Fig. 17.

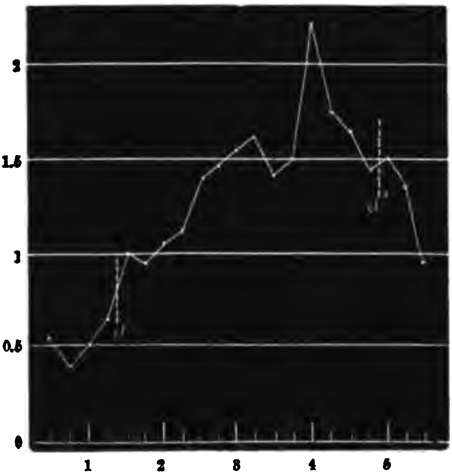


Secretion of bile before and after nitro-hydrochloric acid. 20 cc. water injected into duodenum at *a*. The same with 20 minims dilute nitro-hydrochloric acid injected at *b*, *c*, *d* and *e*.

Autopsy. The duodenal mucous membrane was slightly congested. There was no evidence of purgation.

Experiment 18. Dog that had fasted 17 hours. Weight 17.7 kilogrammes. (Fig. 18.)

Fig. 18.



Secretion of bile before and after nitro-hydrochloric acid. 40 minims dilute nitro-hydrochloric acid in 8 cc. water injected into duodenum at *a*, and again at *a′*.

AUTOPSY. There was slight congestion of the upper part of the small intestine to the extent of about 10 inches. In the duodenum the mucous membrane had a yellowish-grey appearance, as if it had been slightly corroded by an acid. There was no evidence of any purgative effect.

Results of Experiments with Nitro-hydrochloric Acid.—The positive effect of the acid in experiment 18 is a remarkable contrast to the negative result observed in experiment 17. In consequence of the positive result in the latter case, and seeing that it completely agrees with observations on man, we did not think it necessary to perform another experiment. In view of the positive effect in 18, we do not attach any importance to the negative result of experiment 17; for the animal was a small one, and in such a case a cholagogue sometimes fails to act, probably for the reason mentioned at p. 647. It is proved, then, that this acid actually stimulates the hepatic cells. This result is a step in advance of previous knowledge, for observations on man

have not determined whether its cholagogue power is due to reflex stimulation of the gall-bladder, or to excitement of the hepatic secreting apparatus.

ACTION OF MERCURY.

Experiments on the action of calomel have already been detailed in our *first series* (this *Journal*, Vol. x. p. 286). In three of the four experiments there mentioned, calomel caused no increase of the biliary secretion. In the fourth experiment, however, a trivial increase was the result. So many observers having stated that calomel is a cholagogue in the human subject, the result of our experiments seemed to us very remarkable, inasmuch *as every other substance, save ammonium chloride, believed to be a cholagogue in man, is also a cholagogue in the dog.* The harmony existing between the results of our experiments and those of clinical experience, in all cases save those mentioned, induced us to submit the action of mercurial salts to a more searching investigation.

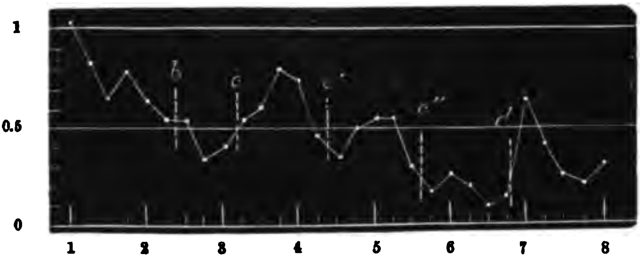
In all the four previous experiments, the calomel was simply suspended in water, and injected into the duodenum. Seeing that it never failed to stimulate the intestinal glands, and thus to produce a purgative action, its negative effect on the liver was the more remarkable. Calomel is insoluble in water, and as Headland (*The Action of Medicines*, 4th edit. London, 1867, p. 380) has pointed out that it is to a slight extent soluble in bile, we are led to suppose that possibly its non-action on the liver in these cases might have resulted from the absence of bile from the intestinal canal. We accordingly performed the two following experiments, in which the calomel was mixed with bile, and then injected into the duodenum.

Experiment 19. Dog that had fasted 17 hours. Weight 14.7 kilogrammes. (Fig. 19.)

AUTOPSY. The upper half of the small intestine contained evidence of decided purgation. Its mucous membrane was considerably congested.

The main result of this experiment was—diminished biliary secretion, nevertheless, the slight increments of secretion that

Fig. 19.

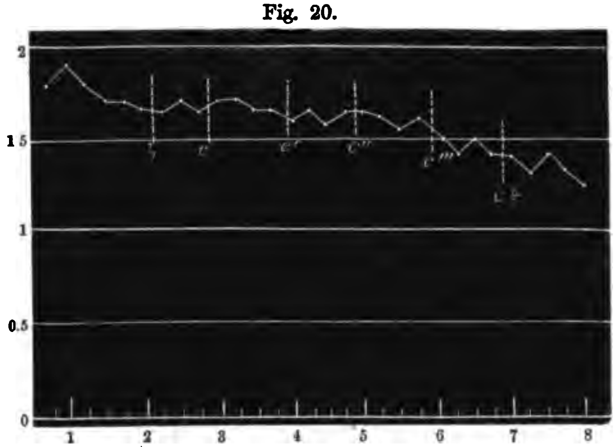


Secretion of bile before and after calomel given with bile. 0.5 cc. bile and 2.5 cc. water injected into duodenum at *b*. 2 grains calomel in the above fluid injected into duodenum at *c*, *c'*, *c''*, and *d*, respectively.

followed the first, second, and fourth doses, rendered a repetition of the experiment desirable.

Experiment 20. Dog that had fasted 17 hours. Weight 25.7 kilogrammes. (Fig. 20.)

Fig. 20.



Secretion of bile before and after calomel given with bile. 0.5 cc. bile and 2.5 cc. water injected into duodenum at *b*. 1 grain calomel in the above fluid injected into duodenum at *c*, *c'*, *c''*, *c'''*, c^4, respectively.

AUTOPSY. The upper half of the small intestine contained 187 cc. of a viscous fluid with grey flakes; thus affording evidence of strong purgation. The vascularity of the mucous membrane was decidedly increased.

Result of Experiments with Calomel mixed with Bile.—The biliary secretion in experiment 20 was so regular, and the

doses of calomel so graduated, that its result may be regarded as conclusively showing, that calomel when mixed with bile and placed in the duodenum, does not excite the liver, although it powerfully stimulates the intestinal glands. *The addition of bile to the calomel made therefore no difference in the result.*

Experiment 18.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.55	
	0.40	0.117 cc.
	0.50	
	0.65	
a		
	1.00	
	0.95	
	1.05	
	1.10	
	1.40	
	1.45	
	1.55	
	1.60	
	1.40	
	1.50	
	2.20	0.392 cc.
	1.72	
	1.62	
	1.45	
a′		
	1.50	
	1.35	
	0.95	

Experiment 19.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.05	
	0.85	
	0.65	
	0.80	
	0.65	
	0.55	
b		
	0.55	0.125 cc.
	0.35	
	0.40	
c		
	0.55	
	0.60	0.196 cc.
	0.80	
	0.75	
	0.45	
c′		
	0.35	
	0.50	
	0.55	0.129 cc.
	0.55	
	0.30	
c″		
	0.15	
	0.25	
	0.20	
	0.10	
	0.15	
d		
	0.65	
	0.40	
	0.25	0.108 cc.
	0.20	
	0.30	

Experiment 20.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.80	
	1.90	
	1.80	
	1.70	
	1.70	
	1.65	
b		
	1.65	0.258 cc.
	1.70	
	1.65	
c		
	1.70	
	1.70	
	1.65	
	1.62	
c′		
	1.60	
	1.62	
	1.57	0.248 cc.
	1.62	
c″		
	1.62	
	1.60	
	1.55	
	1.60	
c‴		
	1.50	
	1.40	
	1.50	
	1.40	
c⁗		
	1.40	
	1.30	
	1.40	0.204 cc.
	1.30	
	1.25	

Since the first series of these experiments was published, some have asked whether the negative effect of the calomel on the liver there recorded, may not have been owing to the

circumstance that the drug was introduced directly into the duodenum, and thus escaped the action of the gastric juice, to which it is subjected when administered by the mouth. As this is the only instance in which our method of administering the various drugs can with the least show of reason be regarded as leading to fallacious results, we resolved to probe this point thoroughly.

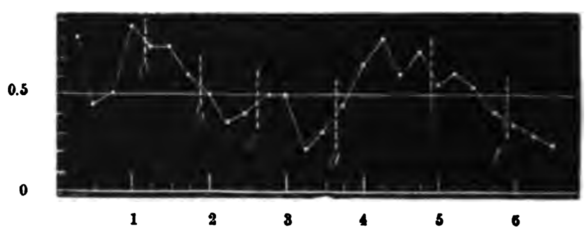
As is well known, Miahle (*Chimie Appliquée*) ascribed all the effects of calomel, and other mercurial preparations, to the production of mercuric chloride, by the action of the alkaline chlorides in the secretions of the alimentary canal, more especially in the gastric juice. This theory has, however, been strongly opposed by Buchheim, Œtinger, and Winckler (referred to in Wood's *Therapeutics*, 1874, p. 330), on the grounds that, at a temperature so low as that of the body, calomel undergoes no transformation into mercuric chloride in a solution of alkaline chlorides. Nevertheless, one must remember that the gastric juice contains free hydrochloric acid. The amount is only 0.02 per cent. in the juice of man, mixed with saliva: in that of the dog, the amount is 0.031 per cent. (C. Schmidt). When Miahle wrote, the free acid of the gastric juice was thought to be lactic; therefore, the effect of very dilute hydrochloric acid on calomel, at the body temperature, has not hitherto been investigated. As no conclusion could be legitimate in the absence of definite information on this point, we performed the following experiment:

Experiment 20 A. Calomel was washed with ether, the filtrate tested with caustic potash, and proved to contain no mercuric chloride. Of the calomel—thus ascertained to be pure—we placed three grammes in 500 cc. distilled water containing 0.02 per cent. anhydrous hydrochloric acid, and submitted the whole to a constant temperature of 100° Fahr.—the temperature of the stomach—for thirty-six hours. The fluid was then filtered, concentrated, and tested with sulphuretted hydrogen. A distinct precipitate—first white, then changing to yellow, and finally to black—was obtained, thus proving the presence of corrosive sublimate. Judging from the precipitate the amount was considerable, but a large quantity of calomel

had been employed, and it had been acted on by the acid for a lengthened period. We repeated the experiment, using the same amount of calomel, and acid fluid, but keeping it only seventeen hours at the temperature of the body. The fluid was then filtered, the filtrate evaporated, the residue dried and weighed, and it was found that 3 grammes of calomel had yielded 17 milligrammes of mercuric chloride. Under similar circumstances, 5 grains calomel—the ordinary dose for a man—would, if digested seventeen hours with about 50 cc. acid fluid, have yielded $\frac{1}{85}$ grain mercuric chloride. Whether or not so minute a quantity of the latter substance is likely to affect the human liver will be considered in the sequel. Calomel is usually taken at bed-time on an empty stomach. We do not know if it can call forth a secretion of gastric juice sufficient to exert an appreciable influence upon it; but in any case, it probably does not remain in the stomach more than five or six hours at the utmost. We however postpone for the present the further consideration of this point.

Experiment 21. Dog that had fasted 17 hours. Weight, 8.8 kilogrammes. (Fig. 21.)

Fig. 21.



Secretion of bile before and after mercuric chloride (corrosive sublimate) given without bile. *a* $\frac{1}{20}$ grain, *b* $\frac{1}{16}$ grain, *c* $\frac{1}{16}$ grain, *d* $\frac{1}{30}$ grain, *e* $\frac{1}{16}$ grain, *f* $\frac{1}{16}$ grain mercuric chloride in 3 cc. water injected into duodenum. ($\frac{3}{8}$ grain given in all.)

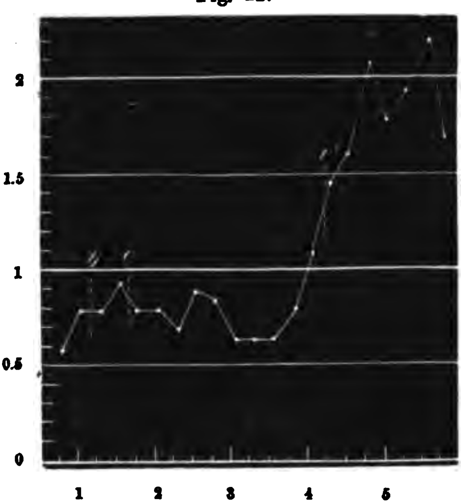
AUTOPSY. The mucous membrane of about fourteen inches of the upper portion of the small intestine was much congested. In the upper part of the duodenum there were minute hæmorrhagic extravasations. There was evidence of a very slight purgative effect.

The increase of secretion that followed the fourth dose of mercuric chloride was so slight, that on the whole, the result

must be regarded as negative. Considering the solubility of mercuric chloride in water,—and the striking contrast between it and calomel in this respect,—it is not at all probable that the negative result in experiment 21 was due to the non-absorption of the mercurial salt. Probably it was simply owing to the circumstance that, in small—somewhat weak dogs—such as that employed in the above experiment, the most certain cholagogues sometimes fail to stimulate the liver, probably because of the depressing effect of the preliminary operation adopted in these experiments. Whatever be the explanation of the result in the preceding case, we resolved in the next, to add some bile to the mercuric chloride solution, in case its presence might facilitate absorption, or, at any rate, in order that the conditions encountered in the intestine in a normal case, might be more exactly imitated.

Experiment 22. Dog that had fasted 19 hours. Weight 16·2 kilogrammes. (Fig. 22.)

Fig. 22.



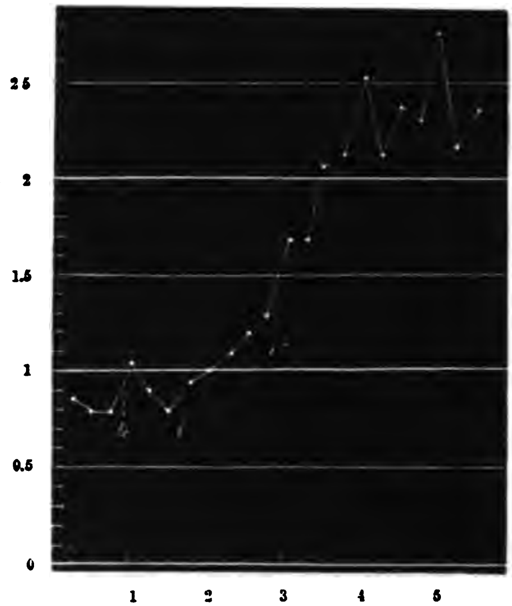
Secretion of bile before and after mercuric chloride given with bile. 0.5 cc. bile and 2.5 cc. water injected into duodenum at *b*. The same fluid with $\frac{1}{16}$ grain mercuric chloride injected into duodenum at *c* and again at *c'* ($\frac{1}{8}$ grain given in all).

AUTOPSY. The mucous membrane of the upper ten inches of the small intestine was decidedly reddened, and there was

evidence of a very slight purgative action in this portion of the intestine.

Experiment 23. Dog that had fasted 19 hours. Weight 17.5 kilogrammes. (Fig. 23.)

Fig. 23.



Secretion of bile before and after mercuric chloride given with bile. *b*, *c*, and *c′* indicate precisely the same as in Fig. 22.

Autopsy. The state of the duodenum and its contents was precisely similar to that described in the preceding experiment.

Experiments 22 and 23 prove conclusively, and in a very striking manner, that mercuric chloride is a hepatic stimulant; and that it is a powerful one is shown by the fact that in experiment 22 $\frac{1}{8}$ grain raised the bile-secretion per kilogramme of body-weight to 0.472 cc. per hour: while in experiment 23 it raised the secretion to 0.557 cc. per kilogramme: per hour.

The contrast between the two last experiments with mercuric chloride and those with calomel is remarkable, both as regards the effect on the *liver*, and on the *intestine;* for while the mercuric chloride powerfully excited the liver, but

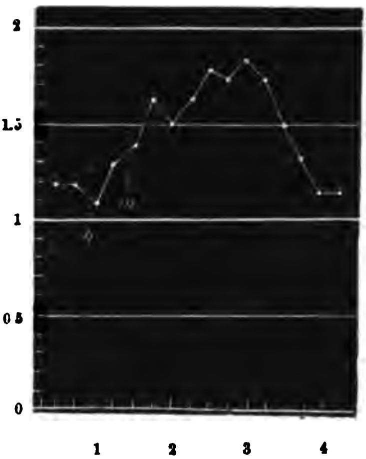
scarcely affected the intestinal glands, notwithstanding its immediate contact with the latter, the calomel did not stimulate the liver, but did powerfully excite the intestinal glands.

This startling result so clearly established by these experiments is a striking proof of the value of this method of investigation as an auxiliary to clinical observations on man.

To render these experiments still more complete, we in the next two cases injected into the duodenum a minute dose of mercuric chloride along with calomel and bile. These experiments are valuable in showing a very remarkable stimulation of the liver that followed an unusually small dose of the mercurial. It should be stated, however, that when we planned the two following experiments we were still under the influence of Miahle's untenable idea before referred to, that mercuric chloride is formed from calomel by the action of the alkaline chlorides of the gastric juice.

Experiment 24. Dog that had fasted 17 hours. Weight 9.9 kilogrammes. (Fig. 24.)

Fig. 24.



Secretion of bile before and after mercuric chloride and calomel given with bile. 0.5 cc. bile and 2 cc. water injected into duodenum at *b*. $\frac{1}{20}$ grain mercuric chloride and 1 grain calomel in the same fluid injected into duodenum at *m*.

AUTOPSY. Slightly increased vascularity of mucous membrane of duodenum. No purgation.

In the above experiment the bile-secretion per hour rose to 0.72 cc. per kilogramme of body-weight, but the secretion was so high—0.48 cc.—before the drug was given, that it was difficult to know exactly how to regard the very high figure first mentioned. Another experiment was therefore desirable.

Experiment 22.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.60	0.171 cc.
	0.80	
b	—	
	0.80	
	0.95	
c	—	
	0.80	
	0.80	
	0.70	
	0.90	
	0.85	
	0.65	
	0.65	
	0.65	
	0.80	
	1.1	
c′	—	
	1.45	
	1.60	
	2.10	
	1.80	0.472 cc.
	1.95	
	2.20	
	1.70	

Experiment 23.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.85	
	0.80	
	0.80	0.202 cc.
b	—	
	1.05	
	0.90	
	0.80	
c	—	
	0.95	
	1.00	
	1.10	
	1.20	
	1.30	
c′	—	
	1.70	
	1.70	
	2.10	
	2.15	
	2.55	
	2.15	
	2.40	
	2.35	0.557 cc.
	2.80	
	2.20	
	2.40	

Experiment 24.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.2	0.48 cc.
	1.2	
b	—	
	1.1	
	1.3	
m	—	
	1.4	
	1.65	
	1.50	
	1.65	
	1.80	0.72 cc.
	1.75	
	1.85	
	1.75	
	1.50	
	1.35	
	1.15	
	1.15	

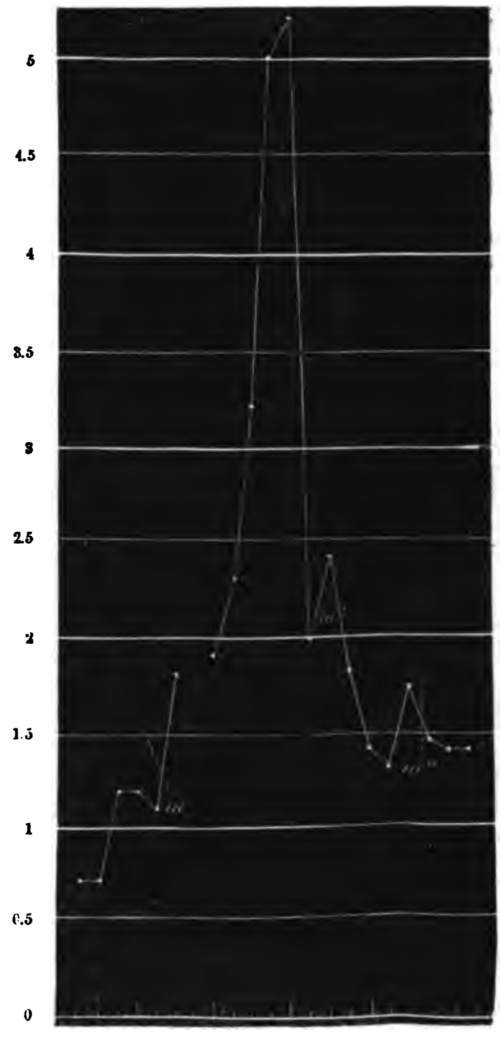
Experiment 25. Dog that had fasted 17 hours. Weight 18.4 kilogrammes. (Fig. 25.)

AUTOPSY. Considerable irritation of the mucous membrane of the upper fourth of small intestine. The contents of this portion of the canal indicated considerable purgative action.

The increase of bile-secretion in experiment 25 is very remarkable, not only for its absolute extent, but also because of the smallness of the dose that occasioned it. The amount of bile secreted per kilogramme of body-weight rose to 0.85 cc. per hour; a very large secretion, that has only been surpassed

in the remarkable experiment with podophylline detailed in the *first series* (this *Journal*, Vol. x. p. 266). (See also Table II. in the sequel.) The effect of so small a dose as $\frac{1}{20}$ grain of mer-

Fig. 25.



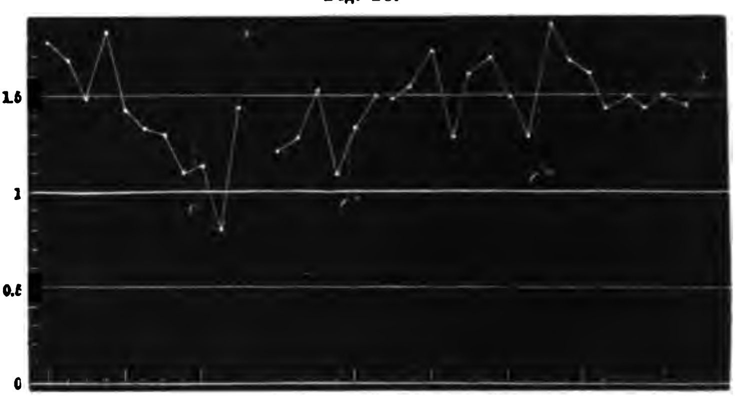
Secretion of bile before and after mercuric chloride and calomel given with bile. $\frac{1}{20}$ grain mercuric chloride with 1 grain calomel in 0.5 cc. bile and 2 cc. water injected into duodenum at *m*, *m'*, and *m''*, respectively.

curic chloride in the last experiment is very remarkable, for the animal was rather larger than those employed in experiments 22 and 23, where $\frac{1}{16}$ and even $\frac{1}{8}$ grain had not so powerful an effect. Considering the result of experiment 20, it is not in the least likely that the addition of one grain of calomel to the dose of the mercuric chloride had anything to do with the difference in the result. We can only suggest, by way of explanation, that possibly in some cases, the liver is more susceptible to a mercurial stimulus than it is in others.

With the mercuric chloride we had given bile in every case save in experiment 21, and that was the only instance where the result was negative; we therefore thought it desirable to perform another experiment, with mercuric chloride given without bile.

Experiment 26. Dog that had fasted 17 hours. Weight 13·4 kilogrammes. (Fig. 26.)

Fig. 26.



Secretion of bile before and after mercuric chloride given without bile. $\frac{1}{4}$ grain mercuric chloride in .6 cc. water injected into duodenum at *c*, *c′* and *c″*. ($\frac{3}{4}$ grain given in all).

AUTOPSY. The upper fourth of the small intestine contained a considerable quantity of somewhat dark fluid, looking as if bile had been injected. Possibly some bile had, in this case, escaped from the bile-ducts into the intestine during the performance of the operation. The presence or absence of bile would have been determined by testing the fluid for bile

pigment, but unhappily a portion set aside for that purpose was lost.

This experiment therefore is inconclusive as regards the point at issue, viz. whether or not mercuric chloride is absorbed from the intestine without the presence of bile. But we felt that it would scarcely be justifiable to perform yet another experiment to settle the point; for it is to the last degree improbable that bile is necessary, and probably no one will feel inclined to maintain that it is.

Experiment 25.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	0.7	
	0.7	
	1.2	
	1.2	0.228 cc.
	1.1	
m	—	
	1.8	
	lost	
	1.9	
	2.3	
	3.2	0.85 cc.
	5.0	
	5.2	
	2.0	
m′	—	
	2.4	
	1.8	
	1.4	
	1.3	
	1.7	
m″	—	
	1.45	
	1.4	
	1.4	

Experiment 26.

	Secretion of bile per 15″.	Secretion of bile per kilogramme of dog: per hour.
	cc.	
	1.80	
	1.70	
	1.50	
	1.85	
	1.45	
	1.35	0.388 cc.
	1.30	
	1.10	
c	—	
	1.15	
	0.80	
	1.45	
	lost	
	1.25	
	1.30	
	1.55	
	1.10	
c′	—	
	1.35	
	1.50	
	1.50	
	1.55	
	1.75	
	1.80	
	1.65	
	1.70	
	1.50	
	1.30	
c″	—	
	1.90	
	1.70	
	1.65	0.50 cc.
	1.45	
	1.50	
	1.45	
	1.60	

Result of Experiments with Mercuric Chloride.—These experiments conclusively prove that mercuric chloride is a powerful hepatic stimulant in the dog. Probably—now that attention is specially directed to the subject—it will also be found to stimulate the liver of man; for a series of experiments, carried out by the Reporter for Hughes Bennett's Committee (*British Association Reports*, 1868, p. 201), showed that the general effects of mercuric chloride on the dog are similar to those observed in man. Doubtless the converse will be found to hold.

In the series of experiments, just referred to, on the production of mercurialism in the dog, the mercuric chloride was always injected subcutaneously, and in two experiments on the action of this substance on the biliary secretion, performed for that committee, the drug was given in the same manner. This mode of administering a substance for the purpose of acting on the liver was faulty, and its results are not fairly comparable with those of the ordinary method, where the substance is placed in the alimentary canal, from which its molecules are absorbed into the radicles of the portal vein, and so pass to the liver in a much more concentrated stream than they possibly can when the substance passes first into the general and then into the portal circulation.

With regard to these two experiments Hughes Bennett stated in the report[1] "that corrosive sublimate when given" [*subcutaneously*] "in small doses, gradually increased in strength, does not augment the biliary secretion, but that it diminishes it the moment the dose reaches a strength sufficient to deteriorate the general health." The latter part of the statement was warranted by the results of both experiments. But the first part, though true as regards one of the experiments, was certainly untrue as regards the other[2], where an unequivocal increase of bile-secretion took place when the dose of mercuric chloride given subcutaneously, was raised from one-sixth grain *once* a day to one-sixth grain *twice* a day[3]. The reporter of the experiments on that occasion overlooked the important fact here stated, and deduced the above general conclusion from

[1] *Lib. cit.* p. 221. [2] *Lib. cit.* Table XIII. p. 212.
[3] *Loc. cit.* June 9 and 10.

misleading results, arrived at by taking the daily average quantity of bile secreted during too prolonged a period.

Results of Experiments with Calomel.—With regard to calomel we have proved the following: (1) That calomel in doses of 10 grains, 5 grains, or 2 grains, several times repeated, when placed, *without bile*, in the duodenum of a fasting dog, produces a purgative effect, varying with the dose; but, so far from increasing the secretion of the bile, only diminishes it; just as happens when any other substance that is not a hepatic stimulant—*e.g.* magnesium sulphate—is administered. (2) That when calomel is *mixed with bile*, and then introduced into the duodenum, there is no difference in the result, even when, as in experiment 20, the calomel is given in 1 grain doses several times repeated, and the chance of acting on the liver, previous to supervention of the depressing effect of purgation, thus allowed. (3) That if 5 grains of calomel be subjected at 100° Fah. for seventeen hours to the action of dilute hydrochloric acid, of the same strength as that of the human gastric juice, not more than $\frac{1}{35}$ grain of mercuric chloride is produced.

The question now arises, seeing that calomel does not usually remain in the human stomach for more than a night, probably not more than from five to six hours, is it likely that even so much as $\frac{1}{35}$ grain of mercuric chloride is produced from the ordinary dose of 5 grains, and if it is, what effect may it be supposed to have on the human liver? It must be borne in mind, however, that we are here on dangerous ground, for we are inclining to reason about the action of the gastric juice itself from experiments on the action of dilute hydrochloric acid, and a solution of alkaline chlorides. Our reasoning may be legitimate enough, but it would clearly be much more conclusive if we could substitute direct experiment for mere inference. We are in a position to do this.

As regards the dog, it is evident that the only link wanting to complete our chain of evidence is, that we should place the calomel in the *stomach* instead of the *duodenum*, and thus render the case analogous to that of the human subject as regards the administration of this drug.

Experiment 27. Into the stomach of a curarized dog, that had fasted the usual time, we injected 5 grains of calomel in water. The injection was made with a fine syringe, through the *gastric wall*, in order that the whole of it might certainly reach the interior of the viscus. Injection through an oesophagus tube was avoided, because a substance so insoluble as calomel would certainly have clung to the interior of the tube, and would thus have been partly lost.

The result of the experiment was entirely negative, both as regards the liver and the intestinal glands. This was readily explained by the fact, that at the autopsy the calomel was found apparently unchanged, enveloped in the mucus of the stomach. The saliva of the dog is peculiar in containing a very large quantity of mucin. As previously stated (this *Journal*, Vol. XI. p. 61), the accumulation of this viscous saliva in the stomach during fasting, is calculated so seriously to interfere with absorption, that we, on this account, in nearly all these experiments, injected the various drugs directly into the duodenum.

We would not however have attempted the preceding experiment had we at the moment recollected that the question at issue had already received a satisfactory answer from the previous experiments of Scott (Beale's *Archives*, Vol. I.), and still more so from the experiments performed by Professor Gamgee and the Reporter for Hughes Bennett's Committee. In these experiments we tied the common bile-duct in the dog, and established a permanent fistulous opening through the fundus of the gall-bladder. When the wound in the abdominal wall had healed we placed a cannula in the fistula and collected—day after day—the whole bile secreted. In order that variations in the secretion might not be occasioned by variations in the amount of food, the animals were as far as possible placed on a fixed diet. After observing the amount of fluid bile and bile solids secreted during three or four days, we caused the animal to *swallow* calomel or *Pilula Hydrargyri*, and observed the amount of bile secreted thereafter. As the result of four experiments it was found (*British Association Reports*, 1868, p. 214) that

"1. *Pil. Hydrargyri*, given in doses that did not produce purgation, caused no increase of the biliary secretion."

"2. Pil. Hydrargyri, given in doses that produced purgation, diminished the biliary secretion."

"3. Calomel, given in doses of $\frac{1}{12}$ grain from six to fourteen times a day, and in doses of two grains from two to six times a day, did not produce purgation or increase the biliary secretion."

"4. Calomel, given in doses[1] that produced purgation, diminished the biliary secretion."

In the experiments, of which these are the results, the calomel was introduced into the stomach, and the animal had its usual diet. *Every opportunity was therefore afforded for a transformation of the calomel into mercuric chloride*—probably indeed a better opportunity than is afforded in the human subject, for the gastric juice of the dog is—as previously stated p. 645—more acid than that of man, and yet we find that the action of the calomel when placed in the stomach of the dog was just the same as when introduced directly into the duodenum. We have proved that $\frac{1}{20}$ grain corrosive sublimate with 1 grain of calomel when placed in the duodenum (experiment 25) can powerfully stimulate the liver of the dog, but we find no reason for entertaining the idea that the amount of mercuric chloride produced by the gastric juice from 5 grains of calomel has any appreciable effect on the liver, for in one of the experiments for Bennett's Committee the amount of calomel placed in the stomach was 10 grains, and it occasioned no increased secretion of bile. (See foot note[1], and also the remarks at p. 646.)

But it may be said, although these facts render it impossible to entertain the idea that the action of calomel is due to the mercuric chloride produced from it by the gastric juice, is it not possible that the entire absence of the bile from the intestine in the case of the experiments of Bennett's Committee interfered with the absorption of the drug, so that while it excited the intestinal glands with which it came directly in contact, it failed to excite the liver because it could not reach it? This objection cannot be entertained. (1) Because

[1] The dose of calomel was 10 grains given on three successive days. On the first it produced "slight" and on the two other days "decided" purgation, but on all days the fluid and the solid bile was diminished.

experiments 19 and 20 of the present series prove that when calomel mixed with bile is placed in the duodenum, it does not stimulate the liver. (2) In the experiments of Bennett's Committee, although the calomel could not possibly encounter bile in the alimentary canal, *a part of it must have been absorbed,* because when given in small doses, frequently repeated, the animal speedily lost its appetite and became extremely unwell, although the doses were too small to produce purgative action.

The conclusion is inevitable, that while corrosive sublimate does—calomel does not—stimulate the liver of the dog, and that when calomel is placed in the stomach of the dog, there is—if the dose be sufficient—the characteristic action on the intestinal glands, but no excitement of the liver. There is therefore no evidence that a purgative dose of calomel, when acted on by the gastric juice, gives rise to mercuric chloride sufficient to exert any appreciable effect on the liver.

Seeing that in these observations we have submitted to direct experiment on the liver of the dog, every substance that has any reputation as a cholagogue in the case of man, and seeing that we have found that, with the exception of ammonium chloride and calomel, they all increase the biliary *secretion* in the dog, it appears to us that the remarkable harmony between the vast majority of our results and those of clinical experience, entitles us to maintain that our experiments with calomel are not to be set aside by the clinical observer, merely because he may be of the opinion that calomel in some way or other increases the *flow* of the bile in man. There has been on the part of some physicians—who in their lamentable ignorance and narrowmindedness imagine that physiological pharmacology studied on a dog, cannot help them to know the action of a drug on man—a tendency to altogether set aside the results of the experiments on calomel because they do not harmonize with their previously entertained opinions. These physicians appear to imagine that they can end the discussion by simply saying "the liver of a dog is not that of a man." That truism cannot be disputed, and we are perfectly willing to admit that it is possible that the human liver may be more or less susceptible than the liver of the dog to the influence

of various substances, but we maintain that up to this time there *is really no discord* between our results and those arrived at by observations on man.

All our experiments concern the *secretion* and *not* the *expulsion* of bile. For the purpose of arriving at *definite* knowledge, we intentionally—in the manner described at the outset of these experiments—threw out of action the *bile-expelling* mechanism, in order that we might have to deal with the *bile-secreting* apparatus only. *We do not profess to have ascertained anything regarding the action of any drug on the bile-expelling mechanism.*

The clinical observer has supplied most valuable information regarding the power of various substances to increase the amount of bile in the dejections. He observes dejections of a clay-colour, he gives five grains of calomel, and further observes that in some cases the dejections thereafter assume their natural appearance. He cannot be certain of the manner in which this result is brought about. For anything he knows, it may be occasioned (1) by stimulation of the hepatic secreting apparatus; or (2) by stimulation of the muscular fibres of the gall-bladder and larger bile-ducts—to wit—the bile-expelling apparatus; or (3) by removing a catarrhal or congested state of the orifice of the common bile-duct, or of the general extent of the larger bile-ducts; or (4) by removing from the intestine substances which had been passing therefrom into the portal vein and depressing the action of the hepatic cells; or (5) by stimulating the intestinal glands, and thereby producing severe drainage of the portal system, whereby the "loaded" liver might possibly be relieved. Yet notwithstanding the inability of the clinical observer to unravel this complicated web, and supply us with any definite statement, he has felt inclined to think our results of no value[1] merely because we prove by direct experiment that calomel does not in the dog stimulate the hepatic *secreting apparatus*.

Seeing that calomel stimulates the intestinal glands in the dog as in man; seeing that mercury produces salivation, ulceration of gums and other characteristic phenomena in the dog

[1] Vide Dr Moxon's *Hunterian Oration*, 1877, *Medical Press and Circular*, March, 1877.

as in man, the obvious inference is that the reputed cholagogue action of calomel in the human subject is probably not owing to stimulation of the bile-secreting apparatus. And why should we, in the face of our experiments, believe the opposite until the clinical observer substitutes—for *vague conjecture*—definite proof of that opposite, by experimenting in a case of biliary fistula in the human subject, when it happens that no bile enters the intestine.

Our experiments therefore *suggest* that the cholagogue action of calomel in the human subject is to be sought for, not in any supposed power of stimulating the bile-secreting mechanism, but in some one or more of the last *four* modes of action above suggested. Calomel undoubtedly excites the intestinal glands, and for anything we know there may be something peculiar in the nature of its action thereon. For anything we know, it may also have some special influence on the mucous glands and mucous membrane, generally of the larger bile-ducts, whereby a catarrhal condition of these ducts may be relieved and the pent-up bile be thus permitted to escape. There is evidently still abundant room for conjecture, but our experiments plainly narrow its range, and thus contribute to the attainment of definite knowledge.

COMPARATIVE RESULTS OF THE PRECEDING EXPERIMENTS.

Although a fourth series of experiments will be published, it is inexpedient longer to delay a comparative analysis of the preceding experiments, for in them nearly every substance supposed to be a cholagogue has been investigated. It does not however appear necessary to give a tabular analysis of experiments with those substances which have been ascertained to have no notable cholagogue action.

TABLE II.

Series.	Experiment.	Substance given. Name.	Total dose in grains.	Grains per kilogramme of body weight.	Secretion of bile per kilogramme of body weight: per hour. Before	After
					cc.	cc.
I.	1	Normal Secretion of bile during the influence of small doses of Curara.			0.35	
,,	—				0.25	
,,	2				0.15	
,,	8	Podophylline	6 without bile	0.9	0.04	0.47
,,	11	,,	4 with bile	0.23	0.52	1.01
,,	13	Aloes	60 without bile	6.9	0.34	0.69
,,	14	,,	60 ,, ,,	12.0	0.26	0.93
,,	16	Rhubarb	68 ,, ,,	3.06	0.17	0.32
—	—	Senna	135 ,, ,,	5.8	0.21	0.23
,,	22	Colchicum	60 ,, ,,	2.5	0.13	0.45
II.	1	Euonymin	5 with bile	0.21	0.07	0.46
,,	2	,,	5 ,,	0.26	0.25	0.47
,,	3	Sanguinarin	1 ,,	0.05	0.12	0.40
,,	4	,,	3 ,,	0.11	0.16	0.30
,,	5	Iridin	5 ,,	0.22	0.22	0.53
,,	6	,,	5 ,,	0.92	0.16	0.63
,,	8	Leptandria	18 ,,	1.4	0.08	0.31
,,	10	Ipecacuan	60 ,,	2.2	0.24	0.55
,,	11	,,	3 ,,	0.49	0.18	0.38
,,	13	Colocynth	14 ,,	0.53	0.29	0.45
,,	14	,,	7 ,,	0.4	0.16	0.27
,,	15	Jalap	30 ,,	1.2	0.16	0.29
III.	2	Sodium Sulphate	508 ,,	32.3	0.25	0.38
,,	7	Potassium Sulphate	232 without bile	10.7	0.31	0.47
,,	8	Sodium Phosphate	201 ,,	7.4	0.27	0.44
,,	10	Sodic and Potassic Tartrate (Rochelle Salt)	463 with bile	37.0	0.23	0.33
,,	18	Dilute Nitro-hydrochloric acid	36.4 without bile	2.0	0.11	0.39
,,	22	Mercuric chloride	1/8 with bile	0.0077	0.17	0.47
,,	23	,,	1/8 ,,	0.0071	0.20	0.55
,,	24	$HgCl_2$ $HgCl$	1/20 ,, 1 ,,	0.005 0.101	0.48	0.72
,,	25	$HgCl_2$ $HgCl$	1/20 ,, 1 ,,	0.0027 0.054	0.22	0.85

Remarks on Table II.—The high secretion of 0.35 cc. per kilogramme of body-weight per hour in Experiment I. 1, was unusual, seeing that no cholagogue had been administered. The two following experiments give results that much more closely represent the normal secretion in a fasting curarised dog.

The doses of podophylline, aloes and colchicum are excessive, owing to the erroneous impression produced on our minds by Röhrig's research, that the dog requires very large doses. In the other experiments quoted in the Table, the doses were in most instances similar to those employed for a man.

The Table cannot furnish any precise indication of the relative powers of these cholagogues in the human subject, nevertheless it is of much value in showing *approximately* their relative powers as regards the liver of the dog. Speaking broadly—if in a fasting dog, the bile-secretion per hour, for every kilogramme of body-weight, rise to 0·4 cc., the cholagogue may be regarded as a powerful one.

(*To be continued.*)

ERRATA IN THE SECOND SERIES OF EXPERIMENTS.

This Vol. p. 65. Line 12 from top of page. For "boiling water" read *bile and water.*

" " 81. Line 9 from top of page. After the words "into the duodenum at" insert, *b. The same with 7 grains colocynth pulp injected at c.*

DESCRIPTION OF A SULU SKULL, AND SUGGESTIONS FOR CONDUCTING CRANIOLOGICAL RESEARCHES. By PROFESSOR CLELAND, *Galway*.

THE skull about to be described was presented to me by Professor R. O. Cunningham of Belfast, who received it from Navigating Lieutenant Dixon; and it was taken with some other skulls by Lieutenant Dixon from a burial-place in Sulu. It may be considered as a well-authenticated skull of a Sulu Islander. I regret that I have not in my possession more than one specimen, as no one can be more fully conscious than I am of the importance of distinguishing individual peculiarities from those characteristic of races. Yet this one specimen has, I consider, a sufficient number of points of interest to justify its being described.

It is obviously the skull of a male past the prime of life. The lines of suture are all distinct with the exception of those on the palate; but anchylosis has taken place in all those which are exposed to much pressure from the jaws, namely, those of the malar bone, the fronto-maxillary, the pterygo-palatine, spheno-parietal, coronal, and fronto-sphenoidal; while the petrous, squamous, and lambdoidal remain open. It has undergone little gravitation change in the vault, and the dentition has been perfect, although the incisors have dropped out after death. But there are some features of age; the occipital condyles being small and flattened, and little facets present at the back of the foramen magnum where the skull has rested on the arch of the atlas.

It is a heavy skull for its size, weighing 29 ounces, while a massive elderly Irish skull in my possession weighs only 24 ounces. This heaviness depends on great denseness of compact tissue in the thick roof-bones; while, as is often the case in old skulls, other parts are extremely thin; the pars squamosa, the great wing of the sphenoid, and the frontal in front and behind the external angular process being all translucent when held against the light. The frontal sinus is quite rudimentary, although the sphenoidal sinuses are large, and the crista galli of

the ethmoid is hollowed by a small sinus communicating with the middle ethmoid cells.

Examining the exterior, one is struck by a distinct mesial prominence of the frontal bone, amounting to carination, which, however, is smoothed away in the parietal region, leaving there a mere moderate inclination to that roof-shape or ill-filled appearance produced in many savage skulls by flattening above and below the temporal ridges. The position of the place of greatest breadth is similar to that which I have found it to occupy in well-filled skulls, namely, at the point where the squamous suture turns downwards, whereas, in ill-filled or roof-shaped skulls, it is much further up on the parietal bone. The amount of the greatest breadth is 5·3 inches, while the greatest breadth in the course of the coronal suture is the most unusually small amount of 4 inches, a circumstance which is another indication of the preponderance of parietal over frontal development.

The greatest breadth between the zygomatic arches is 5 inches, an amount very distinctly smaller than the extreme breadth of the cranium; and in this respect this skull resembles a Sandwich Islander's which I examined when preparing my memoir on the varieties of the human skull, and differs from the generality of savage skulls, which have the zygomatic breadth either equal to or exceeding the greatest breadth of cranium.

The sockets of the incisor teeth, interfered with on one side by an alveolar abscess, are on the other side seen to be set orthognathously. No lower jaw has been sent, by which to judge the relative directions of the upper and lower incisors; but in the upper jaw there is no indication of prognathous dentition. I use the expression *prognathous dentition* on purpose, as it is important that the old use of the word prognathous, involving, as I showed, a vague and inaccurate reference to a variety of matters other than the position of the teeth, should be avoided. But prognathous dentition is an expression capable of the most rigid accuracy, meaning the meeting of the upper and lower incisors at a distinct angle projecting forwards, and dependent, in its full development, on the projection of the alveolar processes of both jaws forwards.

On the cranium there is a distinctly marked double temporal ridge, to which I may call attention more particularly than I should otherwise do to a circumstance of no national importance, because it is only within recent years that the existence of an upper and a lower ridge has been described. I am indebted to Professor Turner for bringing under my notice on this subject the memoir of Hyrtl[1] who was the first to show that there were two ridges, and a paper by Jhering[2]. That which is ordinarily described as a single ridge really consists of two, and sometimes only one of these is developed, which may be either the upper or the lower; but the ordinary description corresponds most nearly with the lower of the two, and the upper one in part of its course may frequently be confounded with the lower, while it seems at its back part to have escaped notice altogether. The lower temporal ridge starts from the external angular process of the frontal, and marks on the parietal the upper limit of a surface of variable and often considerable breadth roughened in connexion with the origin of the temporal muscle; it reaches the temporal bone at the back of the squamous suture, and may be traced thence to the upper border of the zygoma. The upper ridge extends from the same starting-point in front, and passes about half an inch above the other, and fully an inch behind it, reaching to near the posterior border of the parietal, and is continued downwards and forwards to the line of separation of the rough from the smooth part of the mastoid process. It is this upper ridge which, in the skull now described, reaches at its back part a striking degree of prominence, creating a marked depression on the lower part of the parietal bone. In the upper part this upper ridge, which in many skulls distinctly marks the limit of attachment of temporal fascia, is represented in the skull before me by a mere line and a change in the direction of the Haversian orifices, which outside its circuit are closely set and enter perpendicularly, while within the circuit they are few and slanting. The external pterygoid plate is

[1] Hyrtl, über die doppelten Schläfelinien der Menschenschädel; *Denkschr. der Kaiserl. Akad. d. Wissenschaften*, Wien, 1871.
[2] H. v. Jhering, Schläfenlinien des mensch. Schädels; *Arch. v. Reichert und du Bois-Reymond*, 1875.

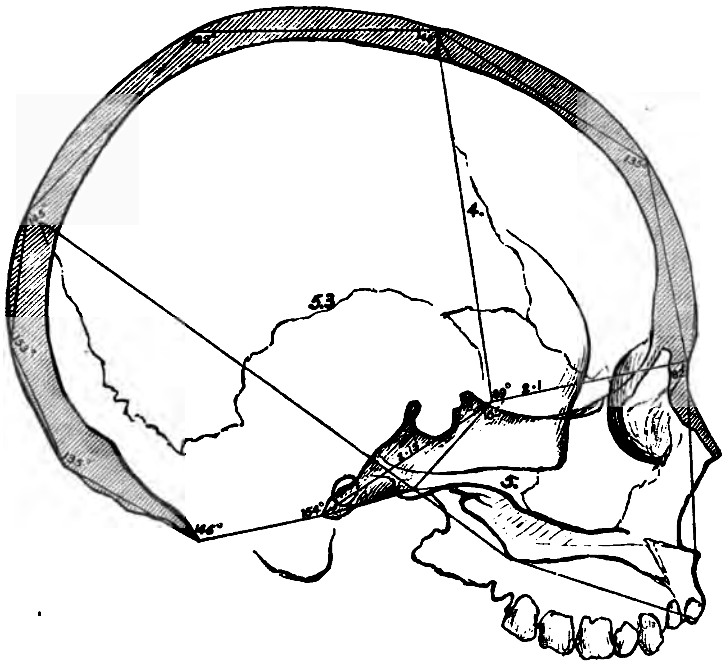
prolonged backwards, so far as to give it a breadth of three quarters of an inch at its broad part; and it seems possible, considering that the Sulu Islanders are grain feeders, that the external pterygoid muscles were largely developed, and that the depression between the two temporal ridges behind denotes a large development of the posterior fibres of the temporal muscle antagonistic to the external pterygoid.

Proceeding now to the mesial characteristics of the cranium, I shall adopt, for the sake of comparison, exactly the same points of measurement as were made use of in my memoir already alluded to[1]; but shall afterwards offer a few remarks on the modifications which might be conveniently introduced in future investigations.

The *base line* from the back of the foramen magnum to the fronto-nasal suture measures 5·4 inches, which is a length such as is often found even in civilized nations, but greater than the average in any civilized nation; and neither the antero-posterior length of the orbit, nor the distance from foramen magnum to the optic foramina, is in any degree excessive. The *arch* is smoothly curved, and measures 14·55, the length being equally distributed between the frontal, parietal, and occipital bones. A comparison of the length of the occipital, parietal, and frontal regions respectively with chords uniting the extremities of each of these regions of the arch, shows that the frontal is slightly more curved than the parietal, and the occipital more curved than either; a character belonging to dolichocephalic forms.

The *length* from the fronto-nasal suture to the occipital probole is 7 inches, and the breadth being, as already mentioned, only 5·3, the percentage proportion of breadth to length, or what has been unadvisedly termed the cephalic index, is 75. But when we come to take the element of *height* into consideration, we find an obvious connexion with the brachycephalic type. The height from the front of the foramen magnum is 5·3; which gives a percentage proportion of height to length approaching to 76, a proportion which lies intermediate between those of skulls distinguished as high and low in my formerly published measurements. Then, when we look at the *radial*

[1] "Inquiry into the Variations of the Human Skull," *Philosophical Transactions*, 1869.



Sulu skull from tracing of a section, with additional details and with measurements after the method described in *Philosoph. Trans.*, 1869.

measurements taken from the post-auricular depression, we get a result associating this skull altogether with the brachycephalic skulls; for on comparing the radii with those published in my memoir, they are seen to have a comparative length peculiar to the brachycephalic form. In that memoir it was shown that four varieties of skull-form might be distinguished by means of those radial measurements, first recommended by Mr Busk: the first group having the radii both in front and behind the mid-parietal point diminishing rapidly, and constituting the thoroughly brachycephalic type; the second with long radii both in front and behind the mid-parietal radius, the thoroughly dolichocephalic type; the third with the radii behind long, and those in front short; and the fourth with the radii in front long and those behind short. The two latter groups require a great amount of further investigation: in my

memoir I did not pretend, with the few skulls which I had for examination, to determine each national form, but only to discover the rules to be followed in making such a determination. Therefore, while I now refer to the four groups which I formerly suggested, I should be sorry to be supposed to have any fixed views as to the nationalities which should be classed in each. But, undoubtedly, in this Sulu skull, the radial measurements, both in front and behind the mid-parietal point, shorten after the fashion of skulls thoroughly brachycephalic. It may be asked, since this is the case, how is it that the proportion of height to length is not more characteristically brachycephalous? And the answer is, that the auditory meatus lies low; its lower border being only about a tenth of an inch higher than the front of the foramen magnum. Altogether, I am inclined to think that, although the arch of the skull has undergone little or no gravitation change, the basilar process has been pressed upwards, thus decreasing the height measured from the front of the foramen magnum.

So far as I may be permitted to form an opinion from a single specimen, I should say that the Sulu skull belongs to the group of short and high skulls not remarkable for breadth, the group *brachycephali angustiores* which I formerly suggested, and to which I refer the Hindoo, the Kanaka, and the New Zealander. It forms a link between that group and the Chinese skull, with which it seems associated by the character of the curve of the arch and the shape of the forehead. It is to be remembered, however, that these remarks are mere suggestions founded on examination of a single skull.

So much for the characters of this one skull. But I certainly should not think of recording at such length the characters of a single skull, had I not reason to believe in the importance of cranial differences in distinguishing nationalities. I am aware that some observers have come to the conclusion that cranial distinctions are so inconstant as to be quite untrustworthy, and indeed such a conclusion is not to be wondered at, when the slovenly way in which skulls are compared is taken into consideration; but I cling to the belief that in every nationality there are numerous cranial characteristics; and that while in any one skull it may happen that one or more of these

are absent, the combined presence of the others would be sufficient, did we study them closely, to distinguish in most instances the nationality.

When one considers what large collections of crania have been made, and the necessity of gathering detailed information from large numbers of specimens in order to reach safe general conclusions, it is provoking to think how meagre the descriptions of specimens in large collections are. I admit that the method which I pursued in inquiring into the general laws of the variations of skulls is too tedious to be applicable to the description of very large numbers; but there is no conceivable reason why Mr Busk's suggestion of radial measurements should not be carried out in every specimen in every large collection; nor is there any reason why the more important step should not be taken of bisecting every skull and obtaining a tracing of it with lithographic chalk, measuring the length of the base-line and its different parts, also the length and chord of each division of the arch, and estimating the more important angles. Such a process would not be tedious; and careful section, instead of diminishing, would add to the value of the specimens.

The principal difficulty in measuring skulls is met with in the basal region; but this region is so important that measurements in which it is left out of consideration are very incomplete; on this account bisection of the skull is advisable, as it furnishes a ready means of subjecting the base to as careful measurement as the roof.

The best plan of measuring a large collection would be to proceed as follows:—

1st. Note any peculiarities of outline, local or general, that meet the eye. Under this head would fall to be noted in the skull just described, the carination of the forehead, and the character of the temporal ridge. It should be noted if the transverse curve of the vault is regular or roof-like, indicating a well- or ill-filled condition with a given superficies of bone. Also any marked asymmetry or local increase or diminution of thickness of wall would fall to be noted under this head.

2nd. The cranial capacity may be taken. I mention this because it is a customary observation, and one without which

a list of measurements would be incomplete; but I do not pretend to think that it is of great importance.

3rd. Measure the greatest breadth, noting its position with reference to the temporo-parietal suture; measure also the greatest breadth in the course of the coronal suture, and the breadth between the zygomatic arches. The position of the point of greatest breadth is highly important, because in well-filled skulls it is close to the squamous suture in the part of its course where it turns downwards behind; only in very ill-filled skulls does it rise high on the parietal bone; while in the lowest forms of skull it may descend to the mastoid process. The coronal breadth is useful as indicating in some measure the breadth of the forehead. The zygomatic breadth ought on no account to be overlooked. In civilized races it is narrower than the greatest breadth of the brain-case, and in women it is often scarcely greater than the coronal breadth; but in savage races it is often greater than the breadth of the brain-case, indicating a large development of the muscles of mastication.

4th. Measure the arch from the back of the foramen magnum to the fronto-nasal suture, noting the extent of its occipital, parietal, and frontal parts. This, however, can be done afterwards from the tracing of the mesial section. Some writers recommend that the foramen magnum should be considered as part of the arch rather than as belonging to the base; and, looking at the matter theoretically, it is easy to justify that procedure: but the foramen magnum comports itself in the human subject as part of the base; and it is necessary so to consider it, on account of its angular relations to the other parts of the base.

5th. Take a series of radial measurements. These I have been in the habit of taking from the post-auricular depression, because it is a definite anatomical point, and, as such, furnished me with a zero point and point of suspension in making measurements with my craniometer. It must be admitted, however, that the centre of the auditory meatus, as recommended by Mr Busk, has the advantage, that it permits similar measurements to be made on the living subject.

Having made all these investigations, the next step is an all-important one, which ought on no account to be omitted.

6th. Bisect the skull, and take an accurate tracing of the section by fastening a sheet of paper securely over it, and rubbing with the heel-ball used by shoemakers, or with the similar substance employed for lithographic drawing. Draw lines between definite points on the tracing, and measure the more important distances and angles. Among the more important are the length from the occipital probole to the fronto-nasal suture, and the greatest height from the front of the foramen magnum. But instead of using, as I have hitherto done, the foramen opticum as a point for measuring from; it will be found in any future investigation, of an extended description, more convenient and advantageous to take the posterior edge of the anterior cranial fossa in front of the olivary process of the sphenoid. A line drawn from this to the front of the foramen magnum will nearly correspond with what I have called the foramino-optic line, and might be called the *middle base;* while another carried forwards to the fronto-nasal suture would take the place of what I have termed the orbital length, and might more properly be called the *frontal base.* These lines have a great value in race distinctions, and ought therefore not to be omitted: also, the angular relations of the three portions of the base are important as distinguishing the horizontal and steep varieties of base, a remarkable source of sexual and individual differences of appearance.

It will be well also to draw a line along the cerebral border of the union of the orbital wings of the sphenoid, and to measure the angle between the line so drawn and the frontal base. By this means an indication will be obtained of a peculiarity pertaining specially to certain uncivilized races, in which the orbital wings are depressed in front, while the ethmoid curves upwards as it passes forwards. It is a peculiarity to which I called attention in Australian skulls in consequence of some observations of Landzehrt; and it occurs in the Sulu skull before me.

In every skull examined, the angles of the three great portions of the base one with another should be measured; also

the orbito-frontal and orbito-nasal angles: but the angles obtainable by drawing lines from point to point of the arch also afford valuable information.

By means of any two or more radial measurements, it is obviously easy to obtain the position of the post-auricular depression or central point of the auditory meatus, whichever has been chosen as the starting-point of the radii; and this ought to be marked on the tracing, as it is useful to know the relative positions of the external ear and the front of the foramen magnum.

None but adult male skulls ought to be used in investigating race peculiarities. Feminine sex is a disturbing element: it is always accompanied with arrest of development, and this arrest is of a variable character in different instances. Skulls in which there are evident gravitation changes should also be rejected, or the existence of those changes should be kept in mind in considering the measurements obtained.

An investigation pursued in this manner may seem troublesome; but I press it earnestly on the attention of the few men who have large collections at their disposal, being assured, from the results obtained with my own imperfect opportunities, that the trouble will be amply rewarded by obtaining national distinctions of a most exact description.

Measurements of Sulu Skull, according to the plan now recommended.

Capacity, 85¾ cubic inches.

Breadths: greatest breadth 5.3, situated on the squamous suture 1.9 upwards and a little backwards from it; coronal breadth 4; zygomatic breadth 5.

Arch: occipital 4.7, parietal 5, frontal 4.85, total 14.55.

Base line 5.4.

Proportion of arch to base line 2.69.

Length from occipital probole to fronto-nasal suture 7.

Height 5.3.

Proportion of height to length 75.

Proportion of breadth to length (so-called cephalic index) 75.

Radii from centre of meatus: mid-occipital 3.8; mid-parietal 5.1; mid-frontal 4.7; proportion of mid-occipital and mid-frontal respectively to mid-parietal 78 and 92 p.c.

Portions of base: foramen magnum 2.25; middle base (as recommended for future measurements) 2.05; frontal base 2.35.

Chords: occipital 3.8; parietal 4.6; frontal 4.4.

Angles: between foramen magnum and middle base 146°; between middle and frontal base 146°; between presphenoid level and frontal base 32°; orbito-frontal angle 84° (old system 88°); orbito-nasal 86 (old system 82); mid-parietal angle 132°.

THE DEVELOPMENT OF ELASMOBRANCH FISHES.

By F. M. BALFOUR, M.A., *Fellow of Trinity College, Cambridge.* (Plates XXIV. and XXV.)

(Continued from p. 490.)

THE present Chapter completes the history of the primitive alimentary canal, whose formation has already been described. In order to economise space, no attempt has been made to give a full account of the alimentary canal and its appendages, but only those points have been dealt with which present any features of special interest.

The development of the following organs is described in order.

(1) The solid œsophagus.
(2) The postanal section of the alimentary tract.
(3) The cloaca and anus.
(4) The thyroid body.
(5) The pancreas.
(6) The liver.
(7) The subnotochordal rod.

The solid œsophagus.

A curious point which has turned up in the course of my investigations is the fact that for a considerable period of embryonic life a part of the œsophagus remains quite solid and without a lumen. The part of the œsophagus to undergo this peculiar change is that which overlies the heart, and extends from the front end of the stomach to the branchial region. At first, this part of the œsophagus has the form of a tube with a well-developed lumen like the remainder of the alimentary tract, but at a stage slightly younger than K its lumen becomes smaller, and finally vanishes, and the original tube is replaced by a solid rod of uniform and somewhat polygonal cells. A section of it in this condition is represented in Pl. v. fig. 8*a*.

At a slightly later stage its outermost cells become more columnar than the remainder, and between stages K and L it

loses its cylindrical form and becomes much more flattened. By stage L the external layer of columnar cells is more definitely established, and the central rounded cells are no longer so numerous (Pl. XXIV. fig. 4, *s œs.*).

In the succeeding stage the solid part of the œsophagus immediately adjoining the stomach is carried farther back relatively to the heart and overlies the front end of the liver. A lumen is not however formed in it by the close of stage Q, and beyond that period I have not carried my investigations, and cannot therefore state the exact period at which the lumen reappears. The limits of the solid part of the œsophagus are very satisfactorily shewn in longitudinal and vertical sections.

Up to stage Q there are no signs of a rudimentary air-bladder.

The solidification of the œsophagus belongs to a class of embryological phenomena which are curious rather than interesting, and are mainly worth recording from the possibility of their turning out to have some unsuspected morphological bearings.

The postanal section of the alimentary tract.

An account has already been given of the posterior continuity of the neural and alimentary canals[1], and it was there stated that Kowalevsky was the discoverer of this peculiar arrangement. Since that account was published, Kowalevsky has given further details of his investigations on this point, and more especially describes the later history of the hindermost section of the alimentary tract. He says[2]:

The two germinal layers, epiblast and hypoblast, are continuous with each other at the border of the germinal disc. The primitive groove or furrow appears at the border of the germinal disc and is continued from the upper to the lower side. By the closing of the groove there is formed the medullary canal above, while the part of the groove on the under surface directed below is chiefly converted into the hind end of the alimentary tract. The connection of the two tubes in Acanthias persists till the formation of the anus, and the part of the nervous tube which lies under the chorda passes

[1] *This Journal*, Vol. x. page 681.
[2] *Archiv f. Mic. Anat.* Vol. XIII. pp. 194, 195.

gradually upwards to the dorsal side of the chorda, and persists there for a long time in the form of a large thin-walled vesicle.

The last part of the description beginning at "The connection of" does not hold good for any of the genera which I have had an opportunity of investigating, as will appear from the sequel.

In a previous section[1] the history of the alimentary tract was completed up to stage G.

In stage H the point where the anus will (at a very much later period) appear, becomes marked out by the alimentary tract sending down a papilliform process towards the skin. This is shewn in Vol. x. Pl. xxiv. figs. *H* and *I*, *an*.

That part of the alimentary tract which is situated behind this point may, for convenience, be called *the postanal section*. During stage H the postanal section begins to develope a terminal dilatation or vesicle, connected with the remainder of the canal by a narrower stalk. The relation in diameter between the vesicle and the stalk may be gathered by a comparison of fig. 3*a* and 3*b*, Vol. xi. Pl. v. The diameter of the vesicle represented in section in Pl. v. fig. 3, is 0·328 Mm.

The walls both of the vesicle and stalk are formed of a fairly columnar epithelium. The vesicle communicates in front by a narrow passage (Vol. xi. Pl. v. fig. 3*a*) with the neural canal, and behind is continued into two horns (Vol. xi. Pl. v. fig. 2, *al.*) corresponding with the two caudal swellings spoken of above (Vol. x. p. 557). Where the canal is continued into these two horns, its walls lose their distinctness of outline, and become continuous with the adjacent mesoblast.

In the succeeding stages up to K the tail grows longer and longer, and with it grows the postanal section of the alimentary tract, without however altering in any of its essential characters.

Its features at stage K are illustrated by an optical section of the tail of an embryo (Pl. xxiv. fig. 5) and by a series of transverse sections through the tail of another embryo in Pl. xxiv. fig. 6*a*, 6*b*, 6*c*, 6*d*. In the optical section there is seen a terminal vesicle opening into the neural canal, and con-

[1] *This Journal*, Vol. x. p. 677 et seq.

nected with the remainder of the alimentary tract. The terminal vesicle causes the end of the tail to be dilated, as is shewn in Vol. x. Pl. xxv. fig. *K*. The length of the postanal section extending from the abdominal paired fins to the end of the tail (equal to rather less than one-third of the whole length of the embryo), may be gathered from the same figure.

The most accurate method of studying this part of the alimentary canal is by means of transverse sections. Four sections have been selected for illustration (Pl. xxiv. fig. 6*a*, 6*b*, 6*c*, and 6*d*) out of a fairly-complete series of about one hundred and twenty.

Posteriorly (fig. 6*a*) there is present a terminal vesicle ·25 Mm. in diameter, and therefore rather smaller than in the earlier stage, whose walls are formed of columnar epithelium, and which communicates dorsally by a narrow opening with the neural canal; to this is attached a stalk in the form of a tube, also lined by columnar epithelium, and extending through about thirty sections (Pl. xxiv. fig. 6*b*). Its average diameter is about ·084 Mm. Overlying its front end is the subnotochordal rod (fig. 6*b*, *x*.), but this does not extend as far back as the terminal vesicle.

The thick-walled stalk of the vesicle is connected with the cloacal section of the alimentary tract by a very narrow thin-walled tube (Pl. xxiv. 6*c*, *al*.). This for the most part has a fairly uniform calibre, and a diameter of not more than ·035 Mm. Its walls are formed of a flattened epithelium. At a point not far from the cloaca it becomes smaller, and its diameter falls to ·03 Mm. In front of this point it rapidly dilates again, and, after becoming fairly wide, opens on the dorsal side of the cloacal section of the alimentary canal just behind the anus (fig. 6*d*).

Near the close of stage K at a point shortly behind the anus, where the postanal section of the canal was thinnest in the early part of the stage, the alimentary canal becomes solid (*vide* Vol. xi. Pl. vi. fig. 9*d*), and a rupture here occurs in it at a slightly later period.

In stage L the posterior part of the postanal section of the canal is represented by a small rudiment near the end of the

tail. The rudiment no longer has a terminal vesicle, ***nor does it communicate with the neural canal.*** It was visible in one series for about 40 sections, and was continued forwards by a few granular cells, lying between the aorta and the caudal vein. The portion of the postanal section of the alimentary tract just behind the cloaca, was in the same embryo represented by a still smaller rudiment of the dilated part which at an earlier period opened into the cloaca.

Later than stage L I have failed to find any trace of the postanal section of the alimentary canal, and conclude that it vanishes without becoming converted into any organ in the adult. Since my preliminary account of the development of Elasmobranch Fishes was written, no fresh light appears to have been thrown on the question of the postanal section of the alimentary canal being represented in higher Vertebrata by the allantois.

The cloaca and anus.

Elasmobranchs agree closely with other Vertebrates in the formation of the cloaca and anus, and in the relations of the cloaca to the urinogenital ducts.

The point where the anus, or more precisely the external opening of the cloaca, will be formed, becomes very early marked out by the approximation of the wall of the alimentary tract and external skin. This is shewn for stages H and I in Vol. X. Pl. XXIV. *an.*

Between stages I and K the alimentary canal on either side of this point, which we may for brevity speak of as the anus, is far removed from the external skin, but at the anus itself the lining of the alimentary canal and the skin are in absolute contact. There is, however, no involution from the exterior, but, on the contrary, the position of the anus is marked by a distinct prominence. Opposite the anus the alimentary canal dilates and forms the cloaca.

During stage K, just in front of the prominence of the anus, a groove is formed between two downgrowths of the body-wall. This is shewn in Vol. XI. Pl. VI. fig. 9*a*. During the same stage the segmental ducts grow downwards to the cloaca, and open into it in the succeeding stage (Pl. VI. fig. 9*b*). Up to stage K

the cloaca is connected with the præanal section of the alimentary canal in front, and the postanal section behind; the latter, however, by stage L, as has been stated above, atrophies, with the exception of a very small rudiment. In stage L the posterior part of the cloaca is on a level with the hind end of the kidneys, and is situated behind the posterior horns of the body-cavity, which are continued backwards to about the point where the segmental ducts open into the cloaca, and though very small at their termination rapidly increase in size anteriorly.

Nothing very worthy of note takes place in connection with the cloaca till stage O. By this stage we have three important structures developed. (1) An involution from the exterior to form the mouth of the cloaca or anus. (2) A perforation leading into the cloaca at the hind end of this. (3) The rudiments of the abdominal pockets. All of these structures are shewn in Pl. XXV. fig. 1*a*, 1*b*, 1*c*.

The mouth of the cloaca is formed by an involution of the skin, which is deepest in front and becomes very shallow behind (Pl. XXV. fig. 1*a*, 1*b*). At first only the mucous layer of the skin takes part in it, but when the involution forms a true groove, both layers of the skin serve to line it. At its posterior part, where it is shallowest, there is present, at stage O, a slit-like longitudinal perforation, leading into the posterior part of the cloaca (Pl. XXV. fig. 1*c*) and forming its external opening. Elsewhere the wall of the cloaca and cloacal groove are merely in contact but do not communicate. On each side of the external opening of the cloaca there is present an involution (Pl. XXV. fig. 1*c*, *ab. p.*) of the skin, which quite resembles the median cloacal involution, and forms the rudiment of an abdominal pocket. These two rudiments must not be confused with two similar ones, which are present in all the three sections represented, and mark out the line which separates the limbs from the trunk. These latter are not present in the succeeding stages. The abdominal pockets are only found in sections through the opening into the cloaca, and are only visible in the hindermost of my three sections. It appears, therefore, that all the structures of the adult cloaca are already constituted by stage O, and the subsequent changes, so far as I have investigated them, may be dealt with in very few words. The

perforation of the cloacal involution is carried slowly forwards, so that the opening into the cloaca, though retaining its slit-like character, becomes continuously longer; by stage Q its size is very considerable. The cloacal involution, relatively to the cloaca, recedes backwards. In stage O its anterior end is situated some distance in front of the opening of the segmental duct into the cloaca; by stage P the front end of the cloacal involution is nearly opposite this opening, and by stage Q is situated behind it.

As I have shewn elsewhere[1], the so-called abdominal pores of Scyllium are simple pockets open to the exterior, but without any communication with the body-cavity. By stage Q they are considerably deeper than in stage O, and retain their original position near the hind end of the opening into the cloaca. The opening of the urinogenital ducts into the cloaca will be described in the section devoted to the urinogenital system.

In Elasmobranchs, as in other Vertebrata, that part of the cloaca which receives the urinogenital ducts, is in reality the hindermost section of the gut and not the involution of epiblast which eventually meets this. Thus the urinogenital ducts at first open into the alimentary canal and not to the exterior. This fact is certainly surprising, and its meaning is not quite clear to me.

The very late appearance of the anus may be noticed as a point in which Elasmobranchs agree with other Vertebrata, notably the Fowl[2]. The abdominal pockets, as might be anticipated from their structure in the adult, are simple involutions of the epiblast.

The thyroid body.

The earliest trace of the thyroid body has come under my notice in a Torpedo embryo slightly older than I. In this embryo it appeared as a diverticulum from the ventral surface of the throat in the region of the *mandibular arch*, and extended from the border of the mouth to the point where the ventral aorta divided into the two aortic branches of the mandibular

[1] *This Journal*, Vol. x. p. 34.
[2] Vide Gasser, *Entwicklungsgeschichte der Allantois, etc.*

arch. In front it bounded a groove (Vol. XI. Pl. XVII. fig. 5*a*, *Th.*), directly continuous with the narrow posterior pointed end of the mouth and open to the throat, while behind it became a solid rod attached to the ventral wall of the œsophagus (Pl. XVII. fig. 5*b*, *Th.*). In a Scyllium embryo belonging to the early part of stage K, the thyroid gland presented the same arrangement as in the Torpedo embryo just described, with the exception that no solid posterior section of it was present.

Towards the close of stage K the thyroid body begins to elongate and become solid, though it still retains its attachment to the wall of the œsophagus. The solidification is effected by the columnar cells which line the groove elongating and meeting in the centre. As soon as the lumen is by these means obliterated, small cells make their appearance in the interior of the body, probably budded off from the original columnar cells.

The gland continues to grow in length, and by stage L assumes a long sack-like form with a layer of columnar cells bounding it externally, and a core of rounded cells filling up its interior. Anteriorly it is still attached to the throat, and its posterior extremity lies immediately below the end of the ventral aorta. The cells of the gland contain numerous yellowish concretionary pigment bodies, which are also present in the later stages.

Up to stage P the thyroid gland retains its original position. Its form and situation are shewn in Pl. XXV. fig. 3, in longitudinal and vertical section for a stage between O and P. The external layer of columnar cells has now vanished, and the gland is divided up by the ingrowth of connective-tissue septa into a number of areas or lobules—the rudiments of the future follicles. These lobules are perfectly solid without any trace of a lumen. A capillary network following the septa is present.

By stage Q the rudimentary follicles are more distinctly marked, but still without a lumen, and a connective-tissue sheath indistinctly separated from the surrounding tissue has been formed. My sections do not shew a junction between the gland and the epithelium of the throat; but the two are so close together, that I am inclined to think that such a junction still exists. It is certainly present up to stage P.

Dr Müller[1], in his exhaustive memoir on the thyroid body, gives an account of its condition in two Acanthias embryos. In his earliest embryo (which, judging from the size, is perhaps about the same age as my latest) the thyroid body is disconnected from the throat, yet contains a lumen, and is not divided up into lobules. It is clear from this account, that there must be considerable differences of detail in the development of the thyroid body in Acanthias and Scyllium.

In the Bird Dr Müller's figures shew that the thyroid body developes in the region of the hyoid arch, whereas, in Elasmobranchs, it developes in the region of the mandibular arch. Dr Götte's[2] account of this body in Bombinator accords very completely with my own, both with reference to the region in which it developes, and its mode of development.

The pancreas.

The pancreas arises towards the close of stage K as a somewhat rounded hollow outgrowth from the dorsal side of that part of the gut which from its homologies may be called the duodenum. In the region where the pancreas is being formed the appearances presented in a series of transverse sections are somewhat complicated (Pl. XXIV. fig. 1), owing to the several parts of the gut and its appendages which may appear in a single section, but I have detected no trace of other than a single outgrowth to form the pancreas.

By stage L the original outgrowth from the gut has become elongated longitudinally, but transversely compressed: at the same time its opening into the duodenum has become somewhat narrowed.

Owing to these changes the pancreas presents in longitudinal and vertical section a funnel-shaped appearance (Pl. XXV. fig. 4). From the expanded dorsal part of the funnel, especially from its anterior end, numerous small tubular diverticula grow out into the mesoblast. The apex of the funnel leads into the duodenum. From this arrangement it results that at this period the original outgrowth from the duodenum serves as a receptacle into which each ductule of the embryonic gland opens

[1] *Jenaische Zeitschrift*, Vol. VI.
[2] *Entwicklungsgeschichte d. Unke.*

separately. I have not followed in detail the further growth of the gland. It is, however, easy to note that while the ductules grow longer and become branched, vascular processes grow in between them, and the whole forms a compact glandular body in the mesentery on the dorsal side of the alimentary tract, and nearly on a level with the front end of the spiral valve. The funnel-shaped receptacle loses its original form, and elongating, assumes the character of a duct.

From the above account it follows that the glandular part of the pancreas, and not merely its duct, is derived from the original hypoblastic outgrowth from the gut. This point is extremely clear in my preparations, and does not, in spite of Schenk's observations to the contrary[1], appear to me seriously open to doubt.

The liver.

The liver arises during stage I as a ventral outgrowth from the duodenum immediately in front of the opening of the umbilical canal (duct of the yolk-sack) into the intestine. Almost as soon as it is formed this outgrowth developes two lateral diverticula opening into a median canal.

The two diverticula are the rudimentary lobes of the liver, and the median duct is the rudiment of the common bile-duct (ductus choledochus) and gall-bladder (Vol. XI. Pl. VI. fig. 9).

By stage K the hepatic diverticula have begun to bud out a number of small hollow knobs. These rapidly increase in length and number, and form the so-called hepatic cylinders. They anastomose and unite together, so that by stage L there is constructed a regular network. As the cylinders increase in length their lumen becomes very small, but appears never to vanish (Vol. XI. Pl. XXV. fig. 5).

The mode of formation of the liver parenchyma by hollow and not solid outgrowths agrees with the suggestion made in the *Elements of Embryology*, p. 133, and also with the results of Götte on the Amphibian liver. Schenk has thrown doubts upon the hypoblastic nature of the secreting tissue of the liver, but it does not appear to me, from my own investigations, that this point is open to question.

[1] *Lehrbuch d. vergleichenden Embryologie.*

Coincidently with the formation of the hepatic network, the umbilical vein (Pl. VI. fig. 9, *u. v.*) which unites with the subintestinal or splanchnic vein (Pl. V. fig. 8 *V.*) breaks up into a series of channels, which form a second network in the spaces of the hepatic network. These vascular channels of the liver appear to me to have from the first distinct walls of delicate spindle-shaped cells, and I have failed to find a stage similar to that described by Götte for Amphibians in which the blood-channels are simply lacunar spaces in the hepatic parenchyma.

The changes of the median duct of the liver are of rather a passive nature. By stage O its anterior end has dilated into a distinct gall-bladder, whose duct receives in succession the hepatic ducts, and so forms the ductus choledochus. The ductus choledochus opens on the ventral side of the intestine immediately in front of the commencement of the spiral valve.

It may be noted that the liver and pancreas are corresponding dorsal and ventral appendages of the part of the alimentary tract immediately in front of its junction with the yolk-sack.

The subnotochordal rod.

The existence of this remarkable body in Vertebrata was first made known by Dr Götte[1], who not only demonstrated its existence, but also gave a correct account of its development. Its presence in Elasmobranchs and mode of development were mentioned by myself in my preliminary account of the development of these fishes[2], and it has been independently observed and described by Professor Semper[3]. No plausible suggestion as to its function has hitherto been made, and it is therefore a matter of some difficulty to settle with what group of organs it ought to be treated. In the presence of this difficulty it seemed best to deal with it in this chapter, since it is unquestionably developed from the wall of the alimentary canal.

At its full growth this body forms a rod underlying the notochord, and has nearly the same longitudinal extension as

[1] *Archiv für Micros. Anatomie*, Bd. v., and *Entwicklungsgeschichte d. Unke.*
[2] *Quarterly Journal of Microscopic Science*, Oct. 1874.
[3] *Stammverwandschaft d. Wirbelthiere u. Wirbellosen* and *Das Urogenitalsystem d. Plagiostomen, Arb. Zool. Zoot. Institut. z. Würzburg*, Bd. 11.

this. It is indicated in most of my sections by the letter x. We may distinguish two sections of it, the one situated in the head, the other in the trunk. The junction between the two occurs at the hind border of the visceral clefts.

The section in the trunk is the first to develope. It arises during stage H in the manner illustrated in Vol. XI. Plate V. figs. 1 and 1*a*. The wall of the alimentary canal becomes thickened (Pl. V. fig. 1) along the median dorsal line, or else produced into a ridge into which there penetrates a narrow prolongation of the lumen of the alimentary canal. In either case the cells at the extreme summit of the thickening become gradually constricted off as a rod, which lies immediately dorsal to the alimentary tract, and ventral to the notochord. The shape of the rod varies in the different regions of the body, but it is always more or less elliptical in section. Owing to its small size and soft structure it is easily distorted in the process of preparing sections.

In the hindermost part of the body its mode of formation differs somewhat from that above described. In this part the alimentary wall is very thick and undergoes no special growth prior to the formation of the subnotochordal rod; on the contrary, a small linear portion of the wall becomes scooped out along the median dorsal line, and eventually separates from the remainder as the rod in question. In the trunk the splitting off of the rod takes place from before backwards, so that the anterior part of it is formed before the posterior.

The section of the subnotochordal rod in the head would appear from my observations on Pristiurus to develope in the same way as in the trunk, and the splitting off from the throat proceeds from before backwards (Vol. XI. Pl. XVII. fig. 4*a*).

In Torpedo, this rod developes very much later in the head than in the trunk; and indeed my conclusion that it developes in the head at all is only based on grounds of analogy, since in my oldest Torpedo embryo (just younger than K) there is no trace of it present. In a Torpedo embryo of stage I the subnotochordal rod of the trunk terminated anteriorly by uniting with the throat. The junction was

effected by a narrow pedicle, so that the rod appeared mushroom-shaped in section, the stalk representing the pedicle of attachment.

On the formation of the dorsal aorta, the subnotochordal rod becomes separated from the wall of the gut and the aorta interposed between the two.

The subnotochordal rod attains its fullest development during stage K. Anteriorly it terminates at a point well in front of the ear, though a little behind the end of the notochord; posteriorly it extends very nearly to the extremity of the tail and is almost co-extensive with the postanal section of the alimentary tract, though it does not quite reach so far back as the caudal vesicle (Pl. XXIV. fig. 6*b*). In stage L it is still fairly large in the tail, though it has begun to atrophy anteriorly. We may therefore conclude that its atrophy, like its development, takes place from before backwards. In the succeeding stages I have failed to find any trace of it, and conclude, as does Professor Semper, that it disappears completely.

Götte[1] is of opinion that the subnotochordal rod is converted into the dorsal lymphatic trunk, and regards it as the anterior continuation of the postanal gut, which he believes to be also converted into a lymphatic trunk. My observations afford no support to these views, and the fact already mentioned, that the subnotochordal rod is nearly co-extensive with the postanal section of the gut, renders it improbable that both these structures are connected with the lymphatic system.

[1] *Entwicklungsgeschichte d. Unke*, p. 775.

The Vascular System and Vascular Glands.

The present chapter deals with the early development of the heart, the development of the general circulatory system, especially the venous part of it, and the circulation of the yolk-sack. It also contains an account of two bodies which I shall call the suprarenal and interrenal bodies, which are generally described as vascular glands.

The heart.

The first trace of the heart becomes apparent during stage G, as a cavity between the splanchnic mesoblast and the wall of the gut immediately behind the region of the visceral clefts (Vol. XI. Pl. V. fig. 4, *ht.*).

The body-cavity in the region of the heart is at first double, owing to the two divisions of it not having coalesced; but even in the earliest condition of the heart the layers of splanchnic mesoblast of the two sides have united so as to form a complete wall below. The cavity of the heart is circumscribed by a more or less complete epithelioid (endothelial) layer of flattened cells, connected with the splanchnic wall of the heart by protoplasmic processes. The origin of this lining layer I could not certainly determine, but its connection with the splanchnic mesoblast suggests that it is probably a derivative of this[1]. In front the cavity of the heart is bounded by the approximation of the splanchnic mesoblast to the wall of the throat, and behind by the stalk connecting the alimentary canal with the yolk-sack.

As development proceeds the ventral wall of the heart becomes bent inwards on each side on a level with the wall of the gut (Plate V. fig. 4), and eventually becomes so folded

[1] From observations on the development of the heart in the Fowl, I have been able to satisfy myself that the epithelioid lining of the heart is derived from the splanchnic mesoblast. When the cavity of the heart is being formed by the separation of the splanchnic mesoblast from the hypoblast, a layer of the former remains close to the hypoblast, but connected with the main mass of the splanchnic mesoblast by protoplasmic processes. A second layer next becomes split from the splanchnic mesoblast, connected with the first layer by the above-mentioned protoplasmic processes. Between these two layers is the cavity of the heart, which soon loses its protoplasmic trabeculæ.

in as to form for the heart a complete muscular wall of splanchnic mesoblast. The growth inwards of the mesoblast to form the dorsal wall of the heart does not, as might be expected, begin in front and proceed backwards, but commences behind and is gradually carried forwards.

From the above account it is clear that I have failed to find in Elasmobranchs any traces of two distinct cavities coalescing to form the heart, such as have been recently described in Mammals and Birds; and this, as well as the other features of the formation of the heart in Elasmobranchs, are in very close accordance with the careful description given by Götte[1] of the formation of the heart in Bombinator. The divergence which appears to be indicated in the formation of so important an organ as the heart between Pisces and Amphibians on the one hand, and Aves and Mammalia on the other, is certainly startling, and demands a careful scrutiny. The most complete observations on the double formation of the heart in Mammalia have been made by Hensen, Götte and Kölliker. These observations lead to the conclusion (1) that the heart arises as two independent splits between the splanchnic mesoblast and the hypoblast, each with an epithelioid (endothelial) lining. (2) *That the heart is first formed at a period when the folding in of the splanchnopleure to form the throat has not commenced, and when therefore it would be impossible for it to be formed as a single tube.*

In Birds almost every investigator since von Baer has detected more or less clearly the coalescence of two halves to form the unpaired heart[2]. Most investigators have however believed that there was from the first an unpaired anterior section of the heart, and that only the posterior part was formed by the coalescence of two lateral halves. Professor His[3], and more recently Kölliker, have stated that there is no such unpaired anterior section of the heart. My

[1] Bischoff has recently stated, *Historisch-kritische Bemerkungen ü. d. Entwickelung d. Säugethiereier*, that Götte has found a double formation of the heart in Bombinator. It may seem bold to question the accuracy of Bischoff's interpretation of writings in his own language, but I have certainly failed to gather this either from Dr Götte's text or figures.

[2] Vide *Elements of Embryology*, Foster and Balfour, pp. 64—66.

[3] *Erste Anlage d. Wirbelthierleibes.*

own recent observations confirm their conclusions as to the double formation of the heart, though I find that the heart has from the first a Λ-shaped form. At the apex of the Λ the two limbs are only separated by a median partition and are not continuous with the aortic arches, which do not arise till a later period[1]. In the Bird the heart thus arises just *behind* the completed throat, and a double formation of the heart appears in fact in all instances to be *most distinctly correlated with the non-closure of the throat*, a non-closure which it must be noted would render it impossible for the heart to arise otherwise than as a double cavity. In the instances in which the heart arises as a single cavity *it is formed subsequently to the complete formation of the throat.* There is thus a double coincidence which renders the conclusion almost certain, *that the formation of the heart as two cavities is a secondary change which has been brought about by variations in the period of the closing in of the wall of the throat.*

If the closing in of the throat were deferred and yet the primitive time of formation of the heart retained, it is clear that such a condition as may be observed in Birds and Mammals must occur, and that the two halves of the heart must be formed widely apart, and only eventually united on the folding in of the wall of the throat. We may then safely conclude that the double formation of the heart has no morphological significance, and does not, as might at first sight be supposed, imply that the ancestral Vertebrate had two tubes in the place of the present unpaired heart. I have spoken of this point at considerable length, on account of the morphological importance which has been attached to the double formation of the heart. But the views above enunciated are not expressed for the first time. In the *Elements of Embryology* we say, p. 64, "The exact mode of development (of the heart) appears according to our present knowledge to be very different in different cases; and it seems probable that the differences are in fact the result of variations in the mode of formation and time of closure

[1] Professor Bischoff (*loc. cit.*) throws doubts upon the double formation of the heart, and supports his views by Dr Foster's and my failure to find any trace of a double formation of the heart in the chick. Professor Bischoff must I think have misunderstood our description, which contains a clear account of the double formation of the heart.

of the alimentary canal." Götte again in his great work[1] appears to maintain similar views, though I do not perfectly understand all his statements. In my review of Kölliker's Embryology[2] this point is still more distinctly enunciated in the following passage: "The primitive wide separation and complete independence of the two halves of the heart is certainly surprising; but we are inclined, provisionally at least, to regard it as a secondary condition due to the late period at which the closing of the throat takes place in Mammals."

The general circulation.

The chief points of interest in connection with the general circulation centre round the venous system. The arterial arches present no peculiarities: the dorsal aorta, as in all other Vertebrates, is at first double (Pl. v. fig. 6 *ao*), and, generally speaking, the arrangement of the arteries accords with what is already known in other forms. The evolution of the venous system deserves more attention.

The cardinal veins are comparatively late developments. There is at first one single primitive vein continuous in front with the heart and underlying the alimentary canal through its præanal and postanal sections. This vein is shewn in section in Pl. v. fig. 8, *V.* It may be called either the subintestinal or splanchnic vein. At the cloaca, where the gut enlarges and comes in contact with the skin, this vein is compelled to bifurcate (Pl. XXIV. fig. 6 *d. v. cau.*), and usually the two branches into which it divides are unequal in size. The two branches meet again behind the cloaca and take their course ventral to the postanal section of the gut and terminate close to the end of the tail, Pl. XXIV. fig. 6 *c. v. cau.* In the tail they form what is usually known as the caudal vein. The venous system of Scyllium or Pristiurus, during the early parts of stage K, presents the simple constitution just described.

Before proceeding to describe the subsequent changes which take place in it, it appears to me worth pointing out the remarkable resemblance which the vascular system of an Elasmobranch presents at this stage to that of an ordinary Annelid

[1] *Entwicklungsgeschichte d. Unke*, p. 779, 780, 781.
[2] *This Journal*, Vol. X. p. 794.

and Amphioxus. It consists, as does the circulatory system, in Annelids, of a neural vessel and an intestinal vessel, the blood flowing backwards in the latter and forwards in the former. The two in Elasmobranchs communicate posteriorly by a capillary system, and in front by the arterial arches, connected like the similar vessels in Annelids with the branchiæ. Striking as is this resemblance, there is a still closer resemblance between the circulation of the Scyllium embryo at stage K and that of Amphioxus. The two systems are in fact identical except in very small details. The subintestinal vessel, absent or only represented by the caudal vein and in part by the ductus venosus in higher Vertebrates and adult Fish, forms the main and only posterior venous trunk of Amphioxus and the embryo Scyllium. The only noteworthy point of difference between Amphioxus and the embryo Scyllium is the presence of a portal circulation in the former, absent at this stage in the latter; but even this is acquired in Scyllium before the close of stage K, and does not therefore represent a real difference between the two types.

The cardinal veins make their appearance before the close of stage K, and very soon unite behind with the unpaired section of the caudal vein (Pl. VI. fig. 9 *b*, *p. ca. v.* and *v.*). On this junction being effected retrogressive changes take place in the original subintestinal vessel. It breaks up in front into a number of smaller vessels; the lesser of the two branches connecting it round the cloaca with the caudal vein first vanishes (Pl. VI. fig. 9 *a*, *v*), and then the larger; and the two cardinals are left as the sole forward continuations of the caudal vein. This latter then becomes prolonged forwards, and the two posterior cardinals open into it some little distance in front of the hind end of the kidneys. By these changes and by the disappearance of the postanal section of the gut the caudal vein is made to appear as a superintestinal and not a subintestinal vessel, and as the direct posterior continuation of the cardinal veins. Embryology proves however that the caudal vein is a true subintestinal vessel[1], and that its connection with the cardinals is entirely secondary.

[1] The morphological importance of this point is considerable. It proves, for instance, that the hæmal arches of the vertebræ in the tail (vide *antea*,

The invariably late appearance of the cardinal veins in the embryo and their absence in Amphioxus leads me to regard them as additions to the circulatory system which appeared in the Vertebrata themselves, and were not inherited from their ancestors. It would no doubt be easy to point to vessels in existing Annelids which might be regarded as their equivalent, but to do so would be in my opinion to follow an entirely false morphological scent.

The circulation of the yolk-sack.

The observations recorded on this subject are so far as I am acquainted with them very imperfect, and in most cases the arteries and veins appear to have been transposed.

Professor Wyman[1], however, gives a short description of the circulation in Raja Batis, in which he rightly identifies the arteries, though he regards the arterial ring which surrounds the vascular area as equivalent to the venous sinus terminalis of the Bird.

The general features of the circulation are clearly portrayed in the somewhat diagrammatic figures of Vol. x. Plate XXVI., in which the arteries are represented red, and the veins blue[2].

I shall follow the figures on this plate in my descriptions.

Fig. 1 represents my earliest stage of the circulation of the yolk-sack. At this stage there is visible a single aortic trunk passing forwards from the embryo and dividing into two branches. No venous trunk could be detected with the simple microscope, but probably venous channels were present in the thickened edge of the blastoderm.

In fig. 2 the circulation was greatly advanced[3]. The blastoderm has now nearly completely enveloped the yolk, and there remains only a small circular space (*yk*) not en-

Journal, pp. 418 and 419) potentially, at any rate, encircle the gut and enclose the body-cavity as completely as ribs which meet in the median ventral line may be said to do anteriorly.

[1] *Memoirs of the American Academy of Arts and Sciences*, Vol. IX.

[2] I may state that my determinations of the arrangement of the circulation were made by actual observation of the flow of the blood under the microscope.

[3] My figure may be compared with that of Leydig, *Rochen und Haie*, Plate III. fig. 6. Leydig calls the arterial ring the sinus terminalis and appears to regard it as venous, but his description is so short that this point is not quite clear.

closed by it. The arterial trunk is present as before, and divides in front of the embryo into two branches which turn backwards and nearly form a complete ring round the embryo. In general appearance it resembles the sinus terminalis of the area vasculosa of the Bird, but in reality bears quite a different relation to the circulation. It gives off branches only on its inner side.

A venous system of returning vessels is now fully developed, and its relations are very remarkable. There is a main venous ring round the thickened edge of the blastoderm, which is connected with the embryo by a single stem which runs along the seam where the edges of the blastoderm have coalesced. Since the venous trunks are only developed behind the embryo, it is only the posterior part of the arterial ring which gives off branches.

The succeeding stage, fig. 3, is also one of considerable interest. The arterial ring has greatly extended, and now embraces nearly half the yolk, and sends off trunks on its inner side along its whole circumference.

More important changes have taken place in the venous system. The blastoderm has now completely enveloped the yolk, and as a result of this, the venous ring no longer exists, but at the point where it vanished there may be observed a number of smaller veins diverging in a brush-like fashion from the termination of the unpaired trunk which originally connected the venous ring with the heart. This point is indicated in the figure by the letter *y*. The brush-like divergence of the veins is a still more marked feature in a blastoderm of a succeeding stage (fig. 4).

The circulation in the succeeding stage (fig. 4) (projected in my figure) only differs in details from that of the previous stage. The arterial ring has become much larger, and the portion of the yolk not embraced (*x*) by it is quite small. Instead of all the branches from the ring being of nearly equal size, two of them are especially developed. The venous system has undergone no important changes.

In fig. 5 the circulation is represented at a still later stage. The arterial ring has come to embrace the whole yolk, and as a result of this, has in its turn vanished as did the venous ring

before it. At this stage of the circulation there is present a single arterial and a single venous trunk. The arterial trunk is a branch of the dorsal aorta, and the venous trunk originally falls into the heart together with the subintestinal or splanchnic vein, but on the formation of the liver enters this and breaks up into capillaries in it. The venous trunk leaves the body on the right side, and the arterial on the left.

The most interesting point to be noticed in connection with the yolk-sack circulation of Scyllium is the fact of its being formed on a completely different type to that of the Amniotic Vertebrates.

THE VASCULAR GLANDS.

There are in Scyllium two structures which have gone under the name of the suprarenal body. The one of these is an unpaired rod-like body lying between the dorsal aorta and the caudal vein in the region of the posterior end of the kidneys. This body I propose to call *the interrenal body*. The other is formed by a series of paired bodies situated dorsal to the cardinal veins on branches of the aorta, and arranged segmentally. These bodies I shall call *the suprarenal bodies*. I propose treating the literature of these bodies together, since they have usually been dealt with in this way, and indeed regarded as parts of the same system. As I hope to shew in the sequel, the origin of these bodies is very different. The interrenal body appears to be developed from the mesoblast; while my researches on the suprarenal bodies confirm the brilliant investigations of Leydig, shewing that they are formed out of the sympathetic ganglia.

The most important investigations on these bodies have been made by Leydig[1]. In his first researches, *Rochen u. Haie*, pp. 71, 72, he gives an account of the position and histology of what is probably my interrenal body[2].

[1] *Rochen und Haie* and *Untersuchung. ü. Fische u. Reptilien*.

[2] I do not feel sure that Leydig's unpaired suprarenal body is really my interrenal body, or at any rate it alone. The point could no doubt easily be settled with fresh specimens, but these I unfortunately cannot at present obtain. My doubts rest partly on the fact that, in addition to my interrenal body, other peculiar masses of tissue (which may be called lymphoid in lieu of a better

The position and relations of the interrenal body vary somewhat according to Leydig in different cases. He makes the following statement about its histology. "Fat molecules form the chief mass of the body, which causes its white, or ochre-yellow colour, and one finds freely embedded in them clear vesicular nuclei." He then proceeds to state that this structure is totally dissimilar to that of the Mammalian suprarenal body, and gives it as his opinion that it is not the same body as this. In his later researches[1] he abandons this opinion, and adopts the view that the interrenal body is part of the same system as the suprarenal bodies to be subsequently spoken of. Leydig describes the suprarenal bodies as paired bodies segmentally arranged along the ventral side of the spinal column situated on the successive arteriæ axillares, and in close connection with one or more sympathetic ganglia. He finds them formed of lobes, consisting of closed vesicles full of nuclei and cells. Numerous nerve-fibres are also described as present. With reference to the real meaning of these bodies he expresses a distinct view. He says[2], "As the pituitary body is an integral part of the brain, so are the suprarenal bodies part of the sympathetic system." He re-affirms with still greater emphasis the same view in his *Fische u. Reptilien.* Though these views have not obtained much acceptance, and the accuracy of the histological data on which they are grounded has been questioned, yet I hope to shew in the sequel not only that Leydig's statements are in the main true, but that development proves his conclusions to have been well founded.

Stannius alludes[3] to both these bodies, and though he does not contribute much to Leydig's previous statements, yet he accepts Leydig's position with reference to the relation of the sympathetic and suprarenal bodies[4].

name) are certainly present around some of the larger vessels of the kidneys which are not identical in structure and development with my interrenal body, and partly that Stannius' statements (to be alluded to directly) rather indicate the existence of a second unpaired body in connection with the kidneys, though I do not fully understand his descriptions.

1 *Fische u. Reptilien*, p. 14.

2 *Rochen u. Haie*, p. 18.

3 *Vergleichende Anatomie*, II. Auflage.

4 Stannius' description is not quite intelligible, but appears to point to the existence of a third kind of body connected with the kidney. From my own observations (vide above), I am inclined to regard it as probable that such a third body exists.

The general text-books of Histology, Kölliker's work, and Eberth's article in Stricker's *Histology*, do not give much information on this subject; but Eberth, without apparently having examined the point, questions the accuracy of Leydig's statements with reference to the anatomical relations of the sympathetic ganglia and suprarenal bodies.

The last author who has dealt with this subject is Professor Semper[1]. He records observations both on the anatomy and development of these organs. His anatomical observations are in the main confirmatory of those of Leydig, but he shews still more clearly than did Leydig the segmental arrangement of the suprarenal bodies. He definitely regards the interrenal and suprarenal bodies as parts of the same system, and states that in many forms they are continuous (p. 228):

"Hier freilich gehen sie bei manchen Formen...in einen Körper ueber, welcher zwischen den Enden d. beiden Nieren liegend dicht an der einfachen Caudalvene sitzt."

With reference to their development he says: "They arise then also completely independently of the kidneys, as isolated segmentally arranged groups of mesoderm cells between the convolutions of the segmental organs; only anteriorly do they stretch beyond them, and extend quite up to the pericardium."

To Semper's statements I shall return, but now pass on to my own observations. The paired suprarenal bodies are dealt with first.

The suprarenal bodies.

My observations on these bodies in the adult Scyllium have only been made with specimens hardened in chromic acid, and there are many points which deserve a fuller investigation than I have been able to give them.

The general position and relations of the suprarenal bodies have been fully given by Leydig and Semper, and I have nothing to add to their statements. They are situated on branches of the aorta, segmentally arranged, and extend on each side of the vertebral column from close behind the heart to the posterior part of the body-cavity. The anterior pair are the

[1] *Urogenitalsystem d. Plagiostomen. Arb. Zool. Zoot. Inst. z. Würzburg*, Vol. II.

largest, and are formed apparently from the fusion of two bodies[1]. When these bodies are examined microscopically, their connection with the sympathetic ganglia becomes at once obvious. Bound up in the same sheath as the anterior one is an especially large ganglion already alluded to by Leydig, and sympathetic ganglia are more or less distinctly developed in connection with all the others. There is however considerable irregularity in the development and general arrangement of the sympathetic ganglia, which are broken up into a number of small ganglionic swellings, on some of which an occasional extra suprarenal body is at times developed. As a rule it may be stated that there is a much smaller ganglionic development in connection with the posterior suprarenal bodies than with the anterior.

The different suprarenal bodies exhibit variations in structure mainly dependent on the ganglion cells and nerves in them, and their typical structure is best exhibited in a posterior one, in which there is a comparatively small development of nervous elements.

A portion of a section through one of these is represented on Pl. xxv. fig. 6, and presents the following features. Externally there is present a fibrous capsule, which sends in the septa, imperfectly dividing up the body into a series of alveoli or lobes. Penetrating and following the septa there is a rich capillary network. The parenchyma of the body itself exhibits a well-marked distinction in the majority of instances into a cortical and medullary substance. The cortical substance is formed of rather irregular columnar cells, for the most part one row deep, arranged round the periphery of the body. Its cells measure on about an average ·03 Mm. in their longest diameter. The medullary substance is more or less distinctly divided into alveoli, and is formed of irregularly polygonal cells; and though it is difficult to give an estimate of their size on account of their irregularity, ·021 Mm. may be taken as probably about the diameter of an average cell. The character of the cortical and medullary cells is nearly the same, and the cells of the two strata appear rather to differ in shape than in any other essen-

[1] There is a very good figure of them in Semper's paper, Pl. xxi. fig. 3.

tial point. The protoplasm of both has a markedly yellow tinge, giving to the suprarenal bodies a yellowish brown colour. The nuclei are small compared to the size of the cells, being about ·009 Mm. in both cortical and medullary cells. In the anterior suprarenal body there is a less marked distinction between the cortical and the medullary layers, and a less pronounced yellow coloration of the whole, than in the posterior bodies. The suprarenal bodies are often partially or completely surrounded by a lymphoid tissue, which is alluded to in the account of their development.

The most interesting features of my sections of the anterior bodies are the relations they bring to light between the sympathetic ganglia and the suprarenal bodies. In the case of one of the posterior suprarenal bodies, a small ganglion is generally found attached to both ends of the body, and invested in the same sheath; in addition to this a certain number of ganglion cells (very conspicuous by their size and other characters) are to be found scattered through the body. In the anterior suprarenal bodies the development of ganglion cells is very much greater. If a section is taken through the region where the large sympathetic ganglion (already mentioned) is attached to the body, one half of the section is composed mainly of sympathetic ganglion cells and nerve fibres, and the other of suprarenal tissue, but the former spread in considerable numbers into the latter. A transverse section through the suprarenal body in front of, or behind this point, is still more instructive. One of these is represented in Pl. XXV. fig. 7. The suprarenal tissue is not inserted, but fills up the whole space within the outline of the body. At one point a nerve (*n*) is seen to enter. In connection with this are a number of ganglion cells, the exact distribution of which has been reproduced. They are scattered irregularly throughout the suprarenal body, but are more concentrated at the smaller than at the large end. It is this small end which, in succeeding sections, is entirely replaced by a sympathetic ganglion. Wavy fibres (which I take to be nervous) are distributed through the suprarenal body in a manner which, roughly speaking, is proportional to the number of ganglion cells. At the large end of the body, where there are few nerve cells, the typical suprarenal structure is more or less retained.

Where the nerve fibres are more numerous at the small end of the section, they give to the tissue a somewhat peculiar appearance, though the individual suprarenal cells retain their normal structure. In a section of this kind the ganglion and nerves are clearly so intimately united with the suprarenal body as not to be separable from it.

The question naturally arises as to whether there are cells of an intermediate character between the ganglion cells and the cells of the suprarenal body. I have not clearly detected any such, but my observations are of too limited a character to settle the point in an adverse sense.

The embryological part of my researches on these bodies is in reality an investigation of later development of the sympathetic ganglia. The earliest stages in the development of these have already been given[1], and I take them up here as they appear during stage L, and shall confine my description to the changes they undergo in the anterior part of the trunk. They form during stage L irregular masses of cells with very conspicuous branches connecting them with the spinal nerves (Pl. XXIV. fig. 2). There may be noticed at intervals solid rods of cells passing from the bodies to the aorta, Pl. XXIV. fig. 2. These rods are the rudiments of the aortic branches to which the suprarenal bodies are eventually attached.

In a stage between M and N the trunks connecting these bodies with the spinal nerves are much smaller and less easy to see than during stage L. In some cases moreover the nerves appear to attach themselves more definitely to a central and inner part of the ganglia than to the whole of them. This is shewn in Pl. XXV. fig. 8, and I regard it as the first trace of a division of the primitive ganglia into a suprarenal part and a ganglionic part. The branches from the aorta have now a definite lumen, and take a course through the centre of these bodies, as do the aortic branches in the adult.

By stage O these bodies have acquired a distinct mesoblastic investment, which penetrates into their interior, and divides it, especially in the case of the anterior bodies, into a number of distinct alveoli. These alveoli are far more distinct in some

[1] *Antea*, pp. 438, 439.

parts of the bodies than in others. The nerve-trunks uniting the bodies with the spinal nerves are (at least in specimens hardened in picric and chromic acids) very difficult to see, and I have failed to detect that they are connected with special parts of the bodies, or that the separate alveoli differ much as to the nature of their constituent cells. The aortic branches to the bodies are larger than in the previous stage, and the bodies themselves fairly vascular.

By stage Q (Pl. xxv. fig. 9) two distinct varieties of cells are present in these bodies. One of these is large, angular, and strikingly resembles the ganglion cells of the spinal nerves at the same period. This variety is found in separate lobules or alveoli on the inner border of the bodies. I take them to be true ganglion cells, though I have not seen them in my sections especially connected with the nerves. The cells of the second variety are also aggregated in special lobules, and are very markedly smaller than the ganglionic cells. They form, I imagine, the cells of the true suprarenal tissue. At this and the earlier stage lymphoid tissue, like that surrounding the suprarenal bodies in the adult, is found adjacent to these bodies.

Stage Q forms my last embryonic stage, and it may perhaps be asked on what grounds I regard these bodies as suprarenal bodies at all and not as simple sympathetic ganglia.

My determination mainly rests on three grounds: (1) That a branch from the aorta penetrates these bodies and maintains exactly the same relations to them that the same branches of the aorta do in the adult to the true suprarenal bodies. (2) That the bodies are highly vascular. (3) That in my last stage they become divided into a ganglionic and a non-ganglionic part, with the same relations as the ganglia and suprarenal tissue in the adult. These grounds appear to me to afford ample justification for my determinations, and the evidence adduced above appears to me to render it almost certain that the suprarenal tissue is a product of the primitive ganglion and not introduced from without, though it is not to be denied that a more complete investigation of this point than it has been possible for me to make would be very desirable.

Professor Semper states that he only made a very slight

embryological investigation of these bodies, and probably has only carefully studied their later stages. He has accordingly overlooked the branches connecting them with the spinal nerves, and has not therefore detected the fact that they develope as parts of the sympathetic nervous system. I feel sure that if he re-examines his sections of younger embryos he will not fail to discover the nerve-branches described by me. His descriptions apart from this point accord fairly well with my own. The credit of the discovery that these bodies are really derivatives of the sympathetic nervous system is entirely Leydig's: my observations do no more than confirm his remarkable observations and well-founded conclusions.

Interrenal body.

My investigations on the interrenal body in the adult are even less complete than those on the suprarenal bodies. I find the body forming a small rod elliptical in section in the posterior region of the kidney between the dorsal aorta and unpaired caudal vein. Some little distance behind its front end (and probably not at its thickest point) it measured in one example, of which I have sections, a little less than a millimetre in its longest diameter. Anteriorly it overlaps the suprarenal bodies, and I failed to find any connection between them and it. On this point my observations do not accord with those of Professor Semper. I have however only been able to examine hardened specimens.

It is, vide Pl. XXIV. fig. 8, invested by a fairly thick tunica propria, which sends in septa, dividing it into rather well-marked lobules or alveoli. These are filled with polygonal cells, which form the true parenchyma of the body. These cells are in my hardened specimens not conspicuous by the number of oil-globules they contain, as might have been expected from Leydig's description[1]. They are rather granular in appearance, and are mainly peculiar from the somewhat large size of the nucleus. The diameter of an average cell is about ·015 Mm., and that of the nucleus about ·01 to ·012. The nuclei are

[1] Perhaps the body I am describing is not identical with Leydig's posterior suprarenal body. I do not, as mentioned above, feel satisfied that it is so from Leydig's description.

remarkably granular. The septa of the body are provided with a fairly rich capillary network.

At the first glance there is some resemblance in structure between the tissues of the suprarenal and interrenal bodies, but on a closer inspection this resemblance resolves itself into both bodies being divided up into lobules by connective-tissue septa. There is in the interrenal body no distinction between cortical and medullary layers as in the suprarenal. The cells of the two bodies have very different characters, as is demonstrated by a comparison of the relative diameters of the nuclei and the cells. The cells of the suprarenal bodies are considerably larger than those of the interrenal (·021 to ·03 as compared to ·015), yet the nuclei of the larger cells of the former body do not equal in size those of the smaller cells of the latter (·009 as compared to ·01).

My observations both on the coarser anatomy and on the histology of the interrenal body in the adult point to its being in no way connected with the suprarenal bodies, and are thus in accordance with the earlier and not the later views of Leydig.

The embryology of this body (under the title of suprarenal body) was first described in my preliminary account of the development of the Elasmobranch Fishes[1]. A short account of its embryonic structure was given, and I stated that although I had not fully proved the point, yet I believed it to be derived from the wall of the alimentary canal. As will be shewn in the sequel this belief was ill-founded, and the organ in question is derived from the mesoblast. Allusion has also been made to it by Professor Semper, who figures it at an early stage of development, and implies that it arises in the mesoblast and in connection with the suprarenal body. It appears at stage K as a rod-like aggregate of mesoblast cells, rather more closely packed than their neighbours, between the two kidneys near their hinder ends (Plate v. fig. 9*a*, *su*). The posterior and best marked part of it does not extend further forwards than the front end of the large intestine, and

[1] *Quarterly Journal of Microscopic Science*, October, 1874.

reaches backwards nearly as far as the hinder end of the kidneys. This part of the body lies between the caudal vein and dorsal aorta.

At about the point where the unpaired caudal vein divides into the two cardinals, the interrenal body becomes less well marked off from the surrounding tissue, though it may be traced forward from a considerable distance in the region of the small intestine. It retains up to stage Q its original extension, but the anterior part becomes quite definite though still of a smaller calibre than the posterior. In one of my examples of stage O the two divisions were separated by a small interval, and not as in other cases continuous. I have not determined whether this was an accidental peculiarity or a general feature. I have never seen any signs of the interrenal body becoming continuous with the suprarenal bodies, though, as in the adult, the two bodies overlap for a considerable distance.

The histology of the interrenal body in the embryonic periods is very simple. At first it is formed of cells differing from those around in being more circular and more closely packed. By stage L its cells have acquired a character of their own. They are still spherical or oval, but have more protoplasm than before, and their nucleus becomes very granular. At the same time the whole body becomes invested by a tunic of spindle-shaped mesoblast cells. By stage O it begins to be divided into a number of separate areas or lobes by septa formed of nucleated fibres. These become more distinct in the succeeding stages up to Q (Pl. xxiv. fig. 7), and in them a fair number of capillaries are formed.

From the above description it is clear that embryology lends no more countenance than does anatomy to the view that the interrenal bodies belong to the same system as the suprarenal, and it becomes a question with which (if of either) of these two bodies the suprarenal bodies of the higher Vertebrata are homologous. This question I shall not attempt to answer in a definite way. My own decided belief is that the suprarenal bodies of Scyllium are homologous with the suprarenal bodies of Mammalia, and a good many points both in their structure and position might be urged in favour of this

view. In the mean time, however, it appears to me better to wait before expressing a definite opinion till the embryonic development of the suprarenal bodies has been worked out in the higher Vertebrata.

EXPLANATION OF PLATE XXIV.

Complete list of reference letters.

Nervous System.

sy. g. sympathetic ganglion. *sp. n.* spinal nerve.
p r. posterior root of spinal nerve. *a r.* antorior root of spinal nerve.
n. c. neural canal.

Alimentary Canal.

al. alimentary canal. *um. c.* umbilical canal.
hp. d. ductus choledochus. *du.* duodenum. *pan.* pancreas.
sp. v. intestine with rudiment of spiral valve. *s. œs.* solid œsophagus.
al. v. caudal vesicle of the postanal gut. *cl. al.* cloacal section of alimentary canal.

General.

mp. muscle-plate.
m p.l. muscle-plate sending a prolongation into the limb.
s t. segmental tube. *s d.* segmental duct. *ca v.* cardinal vein.
v. cau. caudal vein. *ao.* dorsal aorta. *aur.* auricle of heart.
ch. notochord. *p o.* primitive ovum. *ir.* interrenal body.
pp. body-cavity. *ep. pp.* epithelial lining of the body-cavity.
me. mesentery. *t. s.* tail swelling. *x.* subnotochordal rod.

Fig. 1. Transverse section through the anterior abdominal region of an embryo of a stage between K and L. Zeiss B, ocul. 2. Reduced one-third.

The section illustrates the junction of a sympathetic ganglion with a spinal nerve and the sprouting of the muscle-plates into the limbs (*m p. l.*).

Fig. 2. Transverse section through the abdominal region of an embryo belonging to stage L. Zeiss B, ocul. 2. Reduced one-third.

The section illustrates the junction of a sympathetic ganglion with a spinal nerve, and also the commencing formation of a branch from the aorta (still solid) which will pass through the sympathetic ganglion, and forms the first sign of the conversion of part of a sympathetic ganglion into one of the suprarenal bodies.

Fig. 3. Longitudinal and vertical section of an embryo of a stage between L and M, shewing the successive junctions of the spinal nerves and sympathetic ganglia.

Fig. 4. Section through the solid œsophagus during stage L. Zeiss A, ocul. 1. The section is taken through the region of the heart, so that the cavity of the auricle (*aur*) lies immediately below the œsophagus.

Fig. 5. Optical section of the tail of an embryo between stages I and K, shewing the junction between the neural and alimentary canals.

Fig. 6. Four sections through the caudal region of an embryo belonging to stage K, shewing the condition of the postanal section of the alimentary tract. Zeiss A, ocul. 2. An explanation of these figures is given on p. 677.

Fig. 7. Section through the interrenal body of a Scyllium embryo belonging to stage Q. Zeiss C, ocul. 2.

Fig. 8. Portion of a section of the interrenal body of an adult Scyllium. Zeiss C, ocul. 2.

EXPLANATION OF PLATE XXV.

Complete list of reference letters.

NERVOUS SYSTEM.

sp. n. spinal nerve. *sy. g.* sympathetic ganglion. *n.* nerve.

ALIMENTARY CANAL.

cl. cloaca. *in. cl.* cloacal involution. *œ. ep.* œsophageal epithelium. *th.* thyroid body. *pan.* pancreas.

GENERAL.

pp. body cavity. *ca. v.* cardinal vein. *cau. v.* caudal vein. *v. ao.* ventral aorta (anterior continuation of bulbus arteriosus). *aur.* auricle. *ven.* ventricle. *w. d.* Wolffian duct. *o. d.* oviduct. *u.* ureter. *ab. p.* abdominal pocket (pore). *p c.* pericardium. *m. m.* muscles. *s r.* suprarenal body. *ly.* lymphoid tissue.

Fig. 1 *a*, 1 *b*, 1 *c*. Three sections through the cloacal region of an embryo belonging to stage O. Fig. 1 *a* is the anterior of the three sections. Zeiss A, ocul. 2. Reduced one-third.

Fig. 1 *a* shews the cloacal involution at its deepest part abutting on the cloacal section of the alimentary tract.

Fig. 1 *b* is a section through a point somewhat behind this close to the opening of the Wolffian ducts into the cloaca.

Fig. 1 *c* shews the opening to the exterior in the posterior part of the cloaca, and also the rudiments of the two abdominal pockets (*ab. p.*).

Fig. 2. Section through the cloacal region of an embryo belonging to stage P. Zeiss A, ocul. 2.
The figure shews the solid anterior extremity of the cloacal involution.

Fig. 3. Longitudinal vertical section through the thyroid body in a stage between O and P. Zeiss *aa*, ocul. 1.
The figure shews the solid thyroid body (*th.*) connected in front with throat, and terminating below the bulbus arteriosus.

Fig. 4. Pancreas (*pan*) and adjoining part of the alimentary tract in longitudinal section, from an embryo between stages L and M. Zeiss A, ocul. 2.

Fig. 5. Portion of liver network of stage L. Zeiss. C ocul. 2. The section is intended to illustrate the fact that the tubules or cylinders of which the liver is composed are hollow and not solid. Between the liver tubules are seen blood spaces with distinct walls, and blood corpuscles in their interior.

Fig. 6. Section through part of one of the suprarenal bodies of an adult Scyllium hardened in chromic acid. Zeiss C, ocul. 2. The section shews the columnar cells forming the cortex and the more polygonal cells of the medulla.

Fig. 7. Transverse section through the anterior suprarenal body of an adult Scyllium. Zeiss B, ocul. 2. Reduced one-third. The tissue of the suprarenal body has not been filled in, but only the sympathetic ganglion cells which are seen to be irregularly scattered through the substance of the body. The entrance of the nerve (*n*) is shewn, and indications are given of the distribution of the nerve-fibres.

Fig. 8. Section through the sympathetic ganglion of a Scyllium embryo between stages M and N, shewing the connecting trunk between the suprarenal body and the spinal nerve (*sp. n.*), and the appearance of an indication in the ganglion of a portion more directly connected with the nerve. Zeiss D, ocul. 2.

Fig. 9. Section through one of the anterior sympathetic ganglia of an embryo of stage Q, shewing its division into a true ganglionic portion (*sy. g.*), and a suprarenal body (*s r*). Zeiss C, ocul. 2.

ON THE QUANTITATIVE RELATION OF LIGHT TO SENSATION.—A CONTRIBUTION TO THE PHYSIOLOGY OF THE RETINA.—*By* B. THOMPSON LOWNE, F.R.C.S., *Arris and Gale Lecturer on Anatomy and Physiology in the Royal College of Surgeons, Lecturer on Physiology at the Middlesex Hospital; Ophthalmic Surgeon to the Great Northern Hospital.*

NEARLY two years ago, my attention was strongly directed to Fechner's law by the important researches of Mr Dewar and Dr M'Kendrick, and I was thus led to undertake a series of investigations on the relation between sensation and stimulus, in the case of light and the retina.

Fechner, as is well known, regards the numerical relation, between a stimulus and the resulting sensation, as a logarithmic one; that is to say, if the strength of the stimulus be represented by a number, the corresponding sensation will be represented by some multiple of its logarithm.

The nature of this relation is most easily realised by drawing a logarithmic curve, when the abscissæ will be proportionate to the stimuli and the ordinates to the corresponding sensations.

Fechner arrived at this relation by considering a sensation as the sum of a series of increments, each resulting from a corresponding increment of stimulus. The law of the increase of the stimulus being well known to be that every successive increment must be proportionate to the already existing stimulus; for instance, in the case of light, no increase in the already existing stimulus produces any change in the sensation unless it is equal to at least $\frac{1}{100}$ of the intensity of the stimulus in action at the time. These conditions are represented by him in the following equations:

$$\frac{\Delta x}{x} = \Delta s,$$

where x represents the strength of the stimulus and S the intensity of the sensation; and by integration

$$S = c \log x + C,$$

which is Fechner's law.

There is, however, a very important difficulty in adopting Fechner's formula, which, so far as I am aware, has not been hitherto pointed out: it is this, the increments to the sensation are evidently supposed to be equal increments and to bear no definite relation to the already existing sensation; whilst all ordinary stimuli are very far removed from the liminal stimulus: hence if Fechner's formula really represented the true value of a sensation, all ordinary sensations should consist of a vast number of perceptible increments; and by ordinary daylight we ought to be able to distinguish a vastly greater number of shades of grey between black and white than we can by the light of a lamp or an ordinary candle. Now, as any one can soon convince himself, this is not the case; an engraving has a very few gradations of shade in it, generally not more than a dozen, and it has nearly the same appearance with very different degrees of illumination.

There can be no doubt that the smallest possible increment of sensation bears a definite relation to the sensation already existing; that it must be regarded as a variable increment, a function of the sensation, and not as a small unit factor the same in magnitude for all sensations. M. Plateau, I suspect from similar considerations, although I have not been able to find the grounds on which he based his conclusions, gives the following formula: $S = Cx^p$, where p is less than unity, x the intensity of the illumination, and C a constant[1].

And this, as I shall now endeavour to shew, agrees with the results of my own investigations.

It occurred to me that the best method of measurement would be to compare the effect of variable stimuli applied to the elements of the retina with a constant stimulus applied to a given proportion of the elements on a given surface of the retina. I had the honour of publishing the results of these experiments in the Proceedings of the Royal Society[2].

[1] *Bulletin Belgique*, 1872. [2] *Proc. R. Soc.* 1877.

The method adopted was as follows. I used a ruled surface with a known proportion of reserved white in it; this was illuminated by the light from two equal paraffin candles, placed at different distances from it, and its tint was compared with that of a shadow, thrown by an opaque body, upon the white paper at the edge of the ruled surface, the candles being so arranged that the light from one of them illuminated the shadow, whilst that from both illuminated the ruled surface and the white paper surrounding it. The shadow was then rendered equal in tint with the ruled surface, as in Lambert's well-known experiment, by altering the distance of one of the candles; and the relative illumination of the shadow to the white surface surrounding it was determined by the distances of the candles. I found that the proportion of the reserved white in the ruled surface always varied as the square root of the intensity to which the illumination of a wholly white surface had to be reduced to match it.

I found for instance that when the candles were placed at the distances of two and four feet respectively, the lighter shadow, or that illuminated by the nearer candle, corresponded to a shaded surface in which $\frac{1}{10}$ was black, and the darker was somewhat darker than a surface half covered by black lines.

Considering the light thrown on the screen by the nearer candle to have the value of 100 units, that of the more remote candle would be 25 units. The total illumination was therefore 125 units; that of the darker shadow 25, and that of the brighter 100 units: these intensities were similar to those of surfaces illuminated by 125 units in which $\frac{1}{10}$ and $\frac{1}{2\cdot 3}$ of the light was absorbed by black lines[1].

The sensations produced therefore by the surfaces having the ratios of illumination

$$20 : 80 : 100$$

taking $\frac{4}{5}$ of the above numbers, corresponded to those from the surfaces in which

$$\frac{4\cdot 2}{10},\ \frac{9}{10},\ \frac{10}{10}$$

[1] The decimals were estimated, not measured.

were white: or as 4·2 : 9 : 10, the square roots of the luminous intensities in the former case.

A number of experiments gave the same results with sufficient accuracy to establish the law that sensations measured by this method correspond in intensity to the square roots of the luminous intensities.

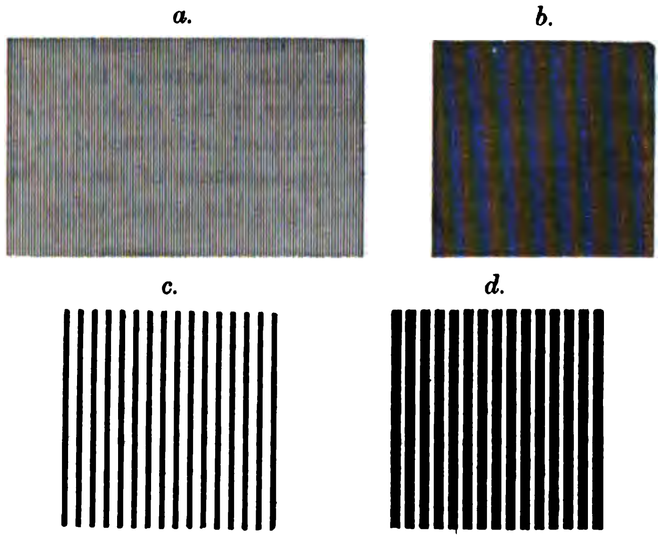
In my earlier experiments I assumed that the number of retinal elements stimulated by any given surface varies as the amount of the surface left uncovered by the black lines ruled upon it. Of course this is only the case when an accurate picture is made upon the retina of such a size that the lines and spaces fall on physiologically distinct elements; the lines need not be mentally distinguished, but are, I believe, always capable of being distinguished as lines by a mental act.

Professor Stokes first pointed out to me the necessity of proving that in my experiments such a picture is actually formed, and of investigating the effect when the lines no longer produce a perfect picture, but become diffused so as to give what is physiologically equivalent to a shadow. He pointed out that if I were right, such a surface should be fainter in shade—that is, it should appear brighter than a ruled surface.

I found this a by no means easy question to settle; but I easily convinced myself that a ruled surface seen slightly out of focus, or by an astigmatic eye, appears lighter than when accurately focused; and this appears to be the case in surfaces of considerable extent, so that it could not be due to the formation of a slightly larger picture. A distant newspaper scarcely differs in appearance from a corresponding sheet of white paper, and two similar prints observed at suitable distances give different tints; the further one, when it no longer produces a distinct picture of the individual lines, appears lighter in tone. Still I did not feel quite satisfied until I succeeded in having the accompanying diagram ruled for me.

The squares *a* and *b*, *c* and *d* have respectively the same proportion of black upon the surface: *a* and *b* are ¼ black, *c* and *d* half black. At suitable distances the following sensations result:—So long as all the lines are distinct there are four distinct shades; *b* and *d* appear darker than *a* and *c* respectively. When the diagram is seen at a distance of from

15 to 20 feet, *c* and *d* become identical in shade and can no longer be separated, but *b* still appears much darker than *a*. At a still greater distance there are but two shades; and these remain distinct so long as the diagram can be distinguished: the illumination is really different; and no distance makes the sensation the same.



I therefore conclude that the intensity of a sensation is represented by the formula

$$S = C\sqrt{x}$$

where S represents the intensity of the sensation and x that of the stimulus: this is clearly only a special form of M. Plateau's law,

$$S = Cx^p.$$

The differential coefficient will of course be represented by $\frac{\Delta x}{\sqrt{x}}$ instead of $\frac{\Delta x}{x}$ as in Fechner's equation.

It is true that the ratio $\frac{\Delta x}{x}$ is that which gives the liminal increment of sensation, but it is an assumption to say that this is a unit increment independent of the already existing sensation. If we use a different definition and suppose that the perceptible increment varies as a function of the already

existing sensation, it appears to me that the facts are correctly expressed. That is, we consider the increment added to or subtracted from the existing sensation as a geometrical and not an arithmetical term.

In other words Fechner makes the assumption that the lengths of the ordinates of the curve representing our sensations increase by a unit increment corresponding to each liminal increment of sensation; that is, he defines a liminal increment of sensation to have the same value whatever the existing sensation: there is nothing, however, in the conditions of the problem to determine this value without additional data which Fechner did not possess: the measurement of the sensations alone can afford these data, and give the actual value of the ordinates.

It appears to me that the error in Fechner's law arises from his having transformed the fraction $\frac{\Delta x}{x}$, which may be regarded as the expression of a physiological fact (*i.e.* that the value of an increment of stimulus must have a certain value, which is a constant ratio to the stimulus, in order that a difference of sensation should result), into a variable representing the rate of increase of the sensation produced.

If the formula I have adopted is used, the number of perceptible increments in any sensation will vary as a simple multiple of the square root of the intensity of the stimulus, producing it, instead of being equal to $\frac{\log x_1}{\log x - \log x_1}$ a very large number when the stimulus is large in comparison with the liminal stimulus. The estimation of the number of perceptible increments of sensation is attended with great difficulties, but from the examination of the number of shades which can be appreciated with various intensities of illumination, I find that it varies inversely as the distance of the source of light when the illuminating source remains unaltered.

I thought it would be desirable to attempt the estimation of the effect of light of considerable intensity on the nerve-elements of the retina; since Fechner's formula rests for its verification on the relation of the old valuations of the magnitudes of the fixed stars and the photometric evaluations of Sir John Herschel and

Steinheil. Fechner found that the photometric evaluations presented the following relation to the magnitudes given by Herschel,

$$M = 1 - 2{\cdot}8540 \log x,$$

and in the case of those given by Steinheil,

$$M = 2{\cdot}3114 - 2{\cdot}3168 \log x,$$

which agree with his formula.

The following method of observation was that which I adopted. I obtained a small but intensely bright point of light by a small intensity coil, between two fine platinum wires; the size of this spark was arranged to be less than a millimeter in diameter, so that when accurately focused on the retina, and seen at a distance of 5 metres at least, the spot of light should only occupy one element of the yellow spot. The distance of the point of light should not then affect its apparent magnitude except in the same manner as the brightness of the fixed stars affects their apparent magnitude: by using two sparks at different distances I found that their apparent magnitudes varied as their distances from the observer. Of course this magnitude was incapable of measurement, it was therefore only estimated; but several persons gave the same or nearly the same estimates.

At first I was very much puzzled at this, because at the time I made these experiments I had not worked out the law I have already given; but I found the following passage in Humboldt's *Cosmos* quoted from Sir John Herschel: "The comparison of the photometric evaluations with those of the vulgar scale has given the singular result that our ordinary stellar magnitudes, 1, 2, 3, etc., decrease in about the same ratio as a star of the first magnitude when removed to the distances 1, 2, 3..., by which its brightness according to the photometric law would attain the values 1, $\frac{1}{4}$, $\frac{1}{9}$, $\frac{1}{16}$. In order, however, to make this accordance still greater it is only necessary to raise our previously adopted stellar magnitudes about half a magnitude, or more accurately considered ·41, so that a star of the 2·00 magnitude would become in future one of the 2·41 magnitude. The determinations of the magnitudes of the stars according

to this rule gives the brightness of the stars (measured photometrically) of the first, second, etc., magnitudes at exactly 1, $\frac{1}{4}$, $\frac{1}{9}$, $\frac{1}{16}$." This agrees therefore with my observations exactly.

There are two other sets of facts, as I have already pointed out elsewhere[1], which tend to the same conclusion.

First, the time required to produce an impression or to obliterate an impression on the retina varies as the square root of the luminous intensity. This was pointed out by Schafhaütl[2] in the case of intermittent luminous impressions.

I have obtained the same result by a series of experiments with revolving discs similar to those used by MM. Delbœuf and Plateau.

A white card disc, 6 inches in diameter, is set into rapid rotation by clockwork. A portion of a sector of the disc is blackened, so that a grey ring appears during rotation: by reducing the breadth of this sector until the ring is no longer visible, and making the experiment by artificial light, I find that the breadth of the sector at the time of disappearance varies as the distance of the source of light, and that by varying the rate of rotation in the inverse ratio of the distance of the light the ring remains just invisible.

I find that if a disc with a portion of a sector, occupying $\frac{1}{200}$ of its circumference, blackened, gives no grey ring with a single candle to illuminate it 10 feet from it when it revolves from 5 to 6 times in a second, by halving the distance of the candle it must revolve from 10 to 12 times in a second before the ring entirely disappears. A white sector on a black disc obeys the same law, but must occupy only $\frac{1}{1000}$ of the circumference of the disc with the same illumination.

I have concluded that when the grey ring ceases to appear the rotation is sufficiently rapid to cause the sector to occupy the same space for too short a time for it to be seen. With a dull light a white streak on a black surface must occupy the same position for about $\frac{1}{5000}$ of a second to be seen at all; but the time varies inversely as the square root of the illumination. A black spot upon a white ground must rotate much more

[1] *Proc. Roy. Soc.*, l. c. [2] *Münch. Abh.* vii. 465.

slowly to be seen. In this case we have to deal with the duration of an exceedingly faint after-image—that of the white surface—during the passage of the black spot. The rate of rotation necessary to obliterate the effect of the black spot varies also inversely as the distance of the illuminating source.

In making these experiments I accidentally found a very beautiful method of exhibiting the phenomenon of a metallic lustre caused by intermitting luminous impressions; by using a white card disc, a quarter covered with dull lampblack, and a moderate velocity of rotation, it is possible to produce all the tints, and the metallic appearance of tempered steel; with certain rates of rotation the results are exceedingly brilliant.

The second set of phenomena to which I have referred are those connected with the electric variations produced by the action of light on the retina. Referring to the paper I have already mentioned by Mr Dewar and Dr M'Kendrick, I find that in a series of experiments on the electric variations of the eye of the frog under the stimulus of light, the variations of the current were as 1 to 8, when the intensity of the stimulus varied as 1 to 64. In several other cases, where they give their results, the correspondence is also very close, and I strongly suspect that the contradictory results in other cases arise from the variation of the size of the luminous image on the retina.

The authors quoted attempt to find a correspondence between Fechner's law and their observations, but this has only been done by the introduction of an arbitrary adjusting constant into Delbœuf's formula

$$C \log \frac{c+x}{k} = S.$$

This constant has been introduced from M. Delbœuf's paper[1], but by some error the unit of measurement has been misconstrued: in the original paper it is given in circular measure as 0·5 of a degree, where a whole circle is the unit of measurement; this has in some way been overlooked, and it has been used by the authors as if it were a fraction of an ordinary unit; its value is therefore taken 360 times too large.

[1] *Bulletin Belgique*, l. c.

I would further remark in this connection that Mr Siemens has found that the alteration of the conductivity of selenium, by the action of light, is a function of the square root of the intensity of the illumination employed; this may be only a coincidence, but I cannot help thinking there is a more important relation between the phenomena.

The above facts appear to me to justify the following theoretical inferences. A ray of homogeneous light has three properties capable of numerical expression.

1. Its velocity of transmission, which is the same whatever its intensity or colour.

2. The periodic time, or what amounts to the same thing, the length of its vibrations, which determines its colour.

3. The amplitude of its vibrations, which determines its intensity.

Beside these there is a directed or vector quantity that determines the position of the point from which it is emitted or reflected, and the direction of the planes which is capable of only partial expression in the case of ordinary light in which its vibrations take place.

It is quite certain that the unaided eye is only capable of perceiving two of these scalar or numerical quantities and one of these vectors. We appreciate three qualities of the ray corresponding to these, namely, colour, intensity and direction.

In order that no misconception may arise, it is necessary to distinguish carefully between the intensity of the light itself and the intensity of the resulting sensation. The physicist defines the intensity of the light in a given area of a surface at right angles to the ray as the energy passing through the surface itself in the unit of time.

This energy has the dimension $\frac{ML^2}{T^2}$. Hence if we write $\frac{ML^2}{T^2}$ to represent the energy passing through the unit surface in the unit of time, whatever the distance of the surface from the luminous source, the surface always remaining at right angles to the ray; we have $D^2 . ML^2 = \text{const.}$ since T^2 remains a constant, therefore $L^2 \propto \frac{1}{D^2}$ (putting M for the mass of the

vibrating particles of ether). From these we may evidently write $\frac{M}{D^2}$ to represent the amount of energy expended in the unit of time, say on the area of a rod or cone. ML will then represent the corresponding momentum, and it is evident this is the same thing as $\frac{M}{D}$ or $\frac{1}{\sqrt{I}}$, according to the usual definition of intensity.

The view that the intensities of our sensations vary as the amplitudes of the vibrations, when the periodic times remain constant, has already been advanced by Mr R. Moon, both in the case of light and sound[1], on the following theoretical ground, "that our sensations can only depend on the displacement of the molecular constituents of the nerve end organs, and the time in which such displacements occur," hence Mr Moon considered that our sensations must have the dimensions of velocity. Mr Moon observes that the only attempt to prove that the ratio of the intensities of our sensations varies as the square of the velocity, assumes that two equal candles give twice the light of one. Of course it is quite clear that the energy set free by the combustion of two candles must be twice as great as that from the combustion of one; this is capable of experimental verification in the case of heat, and it is undoubtedly true in the case of light. Bearing in mind the dimensions of energy we may write MV^2 to represent the energy liberated from one candle in the form of light vibrations, and $2MV^2$ to represent that from two: if we suppose the number of molecules of ether set into vibration in the two cases to be the same, this difference must depend on a difference of velocity; hence the simple amplitude of the vibrations in the two cases will evidently be in the ratio of 1 to $\sqrt{2}$: which corresponds to the magnitude of the corresponding sensations measured in the manner I have indicated. It is quite easy to show that measured by our sensations two candles do not produce twice the impression of one.

[1] *Lond. and Edin. Phil. Mag.* Vol. 44, 45.

It is a matter of common observation that the additional sensation produced by an extra candle, when eight candles, for instance, are already burning, is very slight; whilst the illumination produced by a single candle is very considerable when compared to that of the eight. The relation of the sensations according to the above law would be as

$$1 : 2\cdot83 : 3;$$

and this appears to me to agree with the relative sensations. Under Fechner's law we should have

$$1 : 2 : 2\cdot04,$$

or some similar relation, which would make the difference between the illumination of eight candles differ too little from that of nine. Whilst if we make the energy the measure of our sensations we should have

$$1 : 8 : 9,$$

a relation which is evidently false in comparing the sensations produced by one candle and eight. No one at the present time would, however, probably support this as the true ratio.

Mr Moon's views have, it is true, received much adverse criticism, but all his opponents have apparently mistaken his meaning. Unless I am much mistaken, they all regard the term intensity as having a meaning quite independent of the nerve structures affected; nor has Mr Moon rendered his meaning sufficiently clear. Sir John Herschel writing in 1827 stated that there was nothing to show whether our sensations depend on the amplitude of the vibrations or the square of the vibrations, but he stated that the square must of necessity be adopted, since the square is the only measure admissible, and consistent with the conservation of energy: but it is clear Sir John Herschel regarded the problem from a purely physical point of view, and he uses the term intensity as a measure of energy and not of sensation.

With regard to the variations of the electric current measured by the galvanometer, as we have to do with the measurement of current, and not with the energy expended, we should expect the variations to correspond to the amplitude and not to the square of the amplitude of the vibrations, if we regard the

electric variations as the direct result of the action of the light upon the nerve elements of the retina and proportionate to a function of their intensity.

In conclusion, I would only remark that if we suppose that the vibrations of ether are transferred to the molecular structure of the rods and cones, probably as Prof. Schultze supposes as stationary waves, there has been no reason as yet, except as a matter of theory, to regard the resulting sensation as proportionate to energy rather than momentum; but I have endeavoured to show that it is demonstrated by actual measurement to correspond to the latter and not to the former.

ON THE VASOMOTOR NERVES OF STRIATED MUSCLES. *By* W. H. GASKELL, M.A.[1]

(*From the Physiological Laboratory, Cambridge.*)

IN a former paper[2] I have discussed the variations occurring in the flow of blood through a muscle of the dog under various conditions. Owing to the nature of the experiment, viz. measuring the flow of blood from the muscle-vein when the muscle was at rest and in action, it was only possible to suggest hypotheses to explain the various phenomena that occurred. I have, however, been able to supplement these experiments with microscopic observations of the vessels in a frog's muscle, and so to clear up many points which were doubtful, and at the same time to show more satisfactorily what is the relation between the nerves and vessels of muscles. These experiments and the discussion upon them form the subject of the present paper.

Since the muscle which I have chiefly used for this purpose, viz. the mylohyoid muscle of the frog, has never before, so far as I know, been made use of for the study of the circulation, it will be better to describe shortly my method of preparation and the nature of the circulation that can be observed in this muscle. I chose a simple muscle like this one rather than the tongue, because the circulation in the tongue cannot be considered as merely a blood stream through muscular tissues, for in addition there are present important glandular elements supplied by the same vessels, and also instead of a single nerve there are various nerves of very different characters, so that the whole question of the nature of the nerve-supply to the vascular tissues is here a much more complicated one, than in the case of the muscles of the dog, which I had used in my former experiments; the tongue therefore is not so suitable for the purpose of supplementing those experiments, as the mylohyoid muscle. Besides this, the circulation in the tongue has already been investigated by different observers without much success.

[1] An abstract of this paper was read before the Royal Society, Dec, 1876, see *Proc. R. Soc.*, Vol. xxv.

[2] *Ludwig's Arbeiten*, 1876, and *Journal of Anat. and Phys.* Vol. XI. p. 360.

By cutting through the skin covering the two mylohyoid muscles in the middle line and then laterally up to both rami of the lower jaw, being careful not to wound the larger vessels in the skin, the flaps of skin can be turned back without any loss of blood, and the two mylohyoid muscles are exposed to view; it is then as a rule seen, that the circulations in the two muscles are nearly if not quite distinct from each other; the aponeurosis separating them containing hardly any vessels except the two large median veins which collect part of the blood from each muscle, and which, running along their respective edges of the aponeurosis, usually turn off to join the other main vessels of each muscle close to the articulation of the upper and lower jaw; and it is seen under the microscope, that the capillaries either form loops at the edge of each muscle and run into veins in the substance of that muscle itself, or else run into their respective median vein. Frequently there is only one median vein present, and sometimes none; in any case, however, the two circulations are distinct. Again, each muscle is attached below to the skin by means of a fine fascia, and here too the main vessels of the muscles pass over this fascia only near the articulation of the two jaws, so that the whole middle part is free from vessels of any size, except in cases when the median veins pass directly across the centre, instead of turning to join the other main vessels; this I have not found often to occur. In order now to observe the circulation in, let us say, the right mylohyoid, the main vessels of the left muscle are first tied and then that muscle is cut through by an incision parallel to the middle line and at a convenient distance from it; next the thin fascia at the base of the muscles is cut nearly up to the place where the vessels of the right muscle cross it, and then, lifting up the right muscle by means of the cut portion of the left, the few very fine connective-tissue fibres attached to the under surface of the muscle are carefully separated; it is now easy to turn the right muscle over on to a prepared diaphragm of gutta percha, and fix it in its place by means of pins stuck into the cut portion of the left mylohyoid; in this way all bleeding is avoided, and the muscle to be observed need never even have been touched. If the frog is supported in the requisite position, it is possible in this manner to spread out the

muscle under a microscope, so as to give a flat surface for examination and at the same time to leave the circulation through the muscle absolutely uninjured. When this has been done, the muscle and its vessels can be examined with nearly the highest powers of the microscope.

The position of the nerve supplying the mylohyoid muscle is also very favourable for experimentation, since arising from the mandibular branch of the trigeminal nerve, it crosses over the ramus of the mandible a little above the articulation, and does not approach the main vessels of the muscle until it has entered into the muscle itself; in order, therefore, to prepare a length of nerve sufficient to be isolated on the electrodes, it is only necessary to cut through the masseter and temporal muscles and so to isolate the mandibular branch of the trigeminal nerve, and at the same time, by cutting away the other smaller branches of this nerve to the skin and other muscles, one makes certain that the mylohyoid nerve alone is stimulated. Thus, then, the nerve can be placed on the electrodes, without any bleeding having been caused and without any interference either to the muscle or its vessels; in fact, my usual plan is to prepare and isolate the nerve, before even cutting through the skin over the two mylohyoid muscles.

In order to obtain an accurate representation of the changes in the calibre of any one artery from time to time, I proceeded as follows. Fixing my attention absolutely on the two thin outer edges of the artery under observation, and on the lines on the micrometer scale, I noted and stated aloud the size of the artery every other second, a metronome on the table beating seconds; these numbers were written down by an assistant, who also opened and shut the key between the induction coil and the electrodes, and took note of any remarks that I might make. Since the animal was always curarized and the nerve well isolated on electrodes protected by paraffin, so that there was no trace of muscular contraction even on strong stimulation, it was easy to measure the varying size of the vessel very accurately at intervals of two seconds, and as this was sufficiently rapid to give a very accurate representation of the variations that occur, I never attempted any more rapid measurements than these. Again, since the stimulation was applied by an

assistant and my whole attention was fixed on the artery under observation, I have often noted the measurements of the artery without being aware of the moment when the stimulation commenced or ended, thus obviating any errors that might arise from an expectation of a particular result.

The spaces between the lines of the micrometer scale represented, with the object-lens that I always made use of, $\frac{1}{120}$th mm., and with this lens the blood-corpuscles were very plainly visible, and the transverse striations of the muscular fibres could be easily seen. As therefore a variation in the diameter of an artery amounting to as much as $\frac{1}{120}$th mm. was by this means very appreciable, I attempted to obtain measurements of smaller variations by dividing with the eye each space into four parts, and estimating the diameter of the artery under observation at any time, according as the variation in its size seemed to correspond most nearly to any one of these four divisions. Variations amounting to as much as one-half or three-fourths of a space, i.e. to $\frac{1}{240}$th or $\frac{1}{160}$th mm., are so visible as to admit of measurement, without much possibility of a mistake as to their occurrence; those, however, that amount only to one-fourth of a space, i.e. to $\frac{1}{480}$ mm., are often more doubtful; as however no inferences have been drawn unless the variations amount to nearly $\frac{1}{120}$ mm., this doubt as to the smallest measurements is of no importance. From the values so obtained, I have constructed a number of curves, the ordinates of which represent the size of the artery every two seconds and the abscissæ the time in seconds. Examples of these curves are given in the course of the paper.

As the study of the circulation in this muscle suggests two distinct subjects of enquiry, I have thought it best to divide this paper into two parts; the first part being a continuation of my former paper and therefore treating of the phenomena that occur in the vascular system of striated muscles, the second part dealing rather with the larger question of the nature of vaso-dilator action.

PART I. THE VASCULAR PHENOMENA OF STRIATED MUSCLES.

1. *The Normal circulation in the muscle.*

Upon examining the muscle when prepared as above described with a low power of the microscope, the nerve being untouched, it is seen that, owing to the thinness of the muscle, the small amount of connective tissue, the absence of glandular tissues and pigment cells, the vessels present an appearance peculiarly favourable for measurement with a micrometer eyepiece; for the edges are so clear and sharply defined, that it is easy to measure accurately the outer edge of the smaller arteries, there being no chance of confusion here between the edge of the artery and the surrounding connective tissue, as in the case of the vessels of the web. If the muscle has been carefully prepared, the blood-stream is seen to have the usual axial character, the inert layer being well seen on each side of the rapid central red corpuscular stream; there is no stagnation in any part of the muscle, but throughout, in arteries, capillaries and veins, a very distinct rapid normal blood-flow is present; and it is possible here to observe the circulation for a long period without any inflammatory changes being set up, and without the character of the blood-stream altering to any great extent; in fact, I have observed the variations in the size of an artery for five hours consecutively, and yet at the end of the time the circulation in the muscle was very nearly as good as at the beginning. Often the arteries seem at first to be rather full and dilated, even though the nerve is intact; soon, however, the stream recovers the normal axial character, and remains in this condition for a considerable length of time, or else gradually and slowly becomes thinner and thinner, until at last there is nearly complete stagnation through the muscle; in the latter case it is only necessary to loosen the pins to see again a good circulation return to the muscle; in fact, extreme care must be taken to prevent as much as possible all strain on the muscle in pinning it out. As to the fulness sometimes seen directly after the muscle has been pinned out, I attribute that to the

effects of some slight carelessness in the preparation of the muscle.

Upon examination of an artery for any length of time, the nerve being untouched, it is often seen that its diameter is continually altering in size, the variations differing very greatly in different animals both as to extent and frequency. They differ from the so-called rhythmic contractions, which have been observed in the vessels of the web and other places, in that the artery under observation suddenly and rapidly dilates, the dilatation in some cases being considerable, and then more gradually returns to what appears to be its normal calibre, the dilatation being always accompanied by a greater fulness of the vessel, the axial character of the stream disappearing.

In fact, just as in the arteries of the web the so-called rhythmic contractions present the same appearance as may be produced by slight stimulations at irregular intervals of the sciatic nerve; so here the so-called rhythmic dilatations appear, as we shall see later on, very similar to the effects of a series of slight stimulations of the muscle-nerve; and as in the web and other places, where rhythmic contractions have been observed, they cease as long as the vessel is dilated by section of its nerve, to recommence again as soon as that dilatation begins to subside; so here too the rhythmic dilatations return after the section of the nerve, being in fact often very visible, as Fig. 3 shows.

2. *Effects of section of the nerve.*

Upon removing the skin over the two mylohyoid muscles, it is seen that both muscles are equally pale, and if then one of the muscle-nerves is cut, the corresponding muscle is immediately seen to become redder than the other, the contrast in some cases being exceedingly well marked. If the muscle is first placed under the microscope and the nerve cut while the measurement of the artery under observation continues uninterruptedly, the curve so obtained (see Fig. 1) shows that for a few seconds after section, varying from 5—10 secs., there is no alteration in the size of the vessel either in the direction of dilatation or constriction or in the character of the blood-stream, that then

there ensues a very rapid and considerable dilatation of the artery, which reaches a maximum in about 20—30″ after the section, that this maximum lasts as a rule only a few seconds, and then the artery slowly and gradually returns to its original dimension. During dilatation the blood-stream always loses

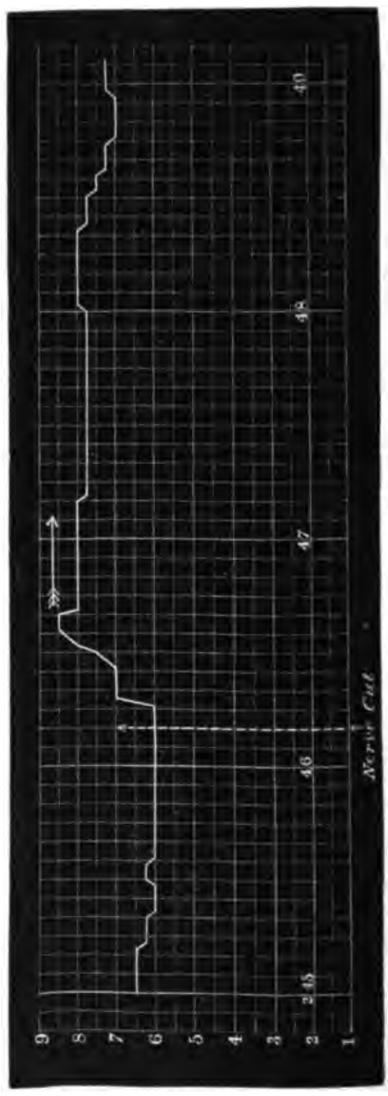


Fig. 1.

Curve showing the effect of section of the nerve.

Measurements of the artery taken every other second. Divisions of the abscissa line represent 5 second intervals. The numbers on the ordinate line correspond to the spaces of the micrometer scale, each unit therefore represents an actual size of $\frac{1}{15}$th mm.

its axial character, the lumen of the vessel becoming filled with corpuscles and the rate of flow at the same time more rapid. Throughout the whole muscle the change is very marked, the capillaries are fuller and distended, the venous flow more rapid, the whole circulation more active; as the dilatation subsides the blood-stream again recovers its normal character.

The length of time the dilatation lasts is, as far as I have seen, very variable; it is possible for the circulation to recover its normal character in from two to four minutes after the section, or, on the other hand, for the dilatation to last in a greater or less degree for nearly the same number of hours. In any case the maximum dilatation, which is reached shortly after the section, is not lasting, the more enduring dilatation being always less than that which occurs soon after section; in other words, section of the nerve always causes a considerable temporary dilatation of the arteries of the muscle, accompanied by a more or less permanent slighter dilatation. In accordance with the views already expressed in my former[1] paper, one might ascribe the more temporary dilatation to a stimulation of vaso-dilator fibres by the mere mechanical action of the section; this view is confirmed by the fact, that any mechanical stimulus such as pinching the peripheral end of the nerve, or still more markedly cutting and tearing it with scissors and forceps, is quite sufficient to cause a rapid temporary dilatation of the artery under observation. However, the fact that the dilatation in these cases is temporary, and never so lasting as that which in some cases follows upon section of the nerve, would tend to show that some further explanation is necessary to account for the more enduring slighter dilatation; and this may be found, as I have suggested in my former paper, in the removal of tonicity owing to the section of vaso-constrictor fibres. On the other hand, I do not attach much value to the cases quoted in that paper, as showing a secondary dilatation after nerve section, for I think, as I have mentioned there, that this dilatation was really due to the placing of the nerve on the electrodes[2], since I have repeatedly observed, that this slight stimulation is quite sufficient to cause a notable dilatation in the arteries of the mylohyoid muscle. However, be that as it

[1] *Op. cit.* [2] *Op. cit.* page 374.

may, the fact still remains, that sometimes the artery under observation remains dilated after section of the nerve a much longer time than it would do, if the effect of section was simply that of a mechanical stimulation.

On the other hand, if section of the nerve simply means removal of tonicity, and the gradual diminution of the original dilatation is due to an increase in the elasticity of the vessel-walls, combined with an increased action of peripheral local centres, owing to the greater supply of blood, then the magnitude of the dilatation caused must signify, that the vaso-constrictor fibres in this nerve are in great abundance, or else very strong in action; and upon this hypothesis, if one compares the marked dilatation caused here by the section of the nerve with the slight dilatation caused in the vessels of the web by the section of the sciatic nerve, one would be led to conclude from this fact alone, that stimulation of the peripheral end of the mylohyoid nerve must necessarily cause a much greater constriction of the arteries of the mylohyoid muscle, than any stimulation of the sciatic could cause in the vessels of the web. However, as is shown later on, the reverse is most markedly the case. A second section of the nerve settles this question, for, however carefully and cleanly the nerve may be cut, there always occurs a marked dilatation presenting the same characters and the same maximum as after the first section, with the single exception, that the normal calibre is sooner reached, the dilatation does not last so long.

It is clear then, that one must consider, in the case of this nerve at all events, that a section of the nerve acts like any other mechanical stimulus, as a strong stimulation to vaso-dilator fibres contained in the nerve, and that possibly in addition the dilatation is made more lasting by the removal of the action of vaso-constrictor fibres at the same time. To this question we shall however again return.

3. *Effects of stimulation of the peripheral end of the nerve.*

In my former paper I have drawn attention especially to the six characteristic variations that occur in the curve representing the outflow of blood from the muscle-vein, before, during, and

after the tetanus of the muscle, and have suggested that the outspurt of blood at the onset of the tetanus and the very brief diminution of flow which occurs at the end of the tetanus, are due to the change of form in the muscle from the relaxed to the contracted state and vice versâ; that the absolute or nearly absolute cessation of flow occurring after the first outspurt is over, is due to the pressure of the contracted muscle or some part of the muscular vascular tract, in conjunction with constriction of the arteries, owing to the stimulation of vaso-constrictor fibres contained in the muscle-nerve, this constriction, as Hafiz[1] noticed, being of but short duration; and that the great increase of flow occurring after a short or during the latter part of a long tetanus, is due to the stimulation of vaso-dilator fibres contained in the nerve.

How far these suggestions are true may be decided by observing with a low power the vessels of the mylohyoid muscle in a slightly curarized frog, and then stimulating the nerve so as to cause a decided tetanus of the muscle. It is then seen, that at the onset of the tetanus there is a momentary forward propulsion of the blood in the larger veins, followed by a complete stoppage of the blood-flow in them, or even by a retrograde flow, while in the arteries, with the exception of an absolutely momentary pause, there is from the very commencement of the tetanus a steady rapid flow; instead of any sign of constriction the arteries steadily dilate, the flow in them is fuller, more rapid, the capillaries become full and distended, and at last, even during the tetanus of the muscle, the flow in the veins after a few spasmodic attempts to move onwards recommences, steadily gaining in force and volume, until on the cessation of the tetanus, there is seen through the whole muscle a stream in arteries, capillaries and veins, much fuller and more rapid than before the commencement of the tetanus; at the end of the tetanus, there is a very momentary stop both in the arterial and venous flow. It is clear then that here the same variations in the rate-curve, as were noticed in the case of the dog, would be obtained, if it were possible to measure the outflow of blood from the vein of the mylohyoid muscle of the frog; and moreover that the explanations given in my former

[1] *Ludwig's Arbeiten*, 1870.

paper[1] to account for the six-fold variation of rate observed, agree with what is here observed except in two particulars. In the first place, the change in the form of the muscle, owing to the tetanus, compresses the larger vein-trunks essentially, and therefore the absolute or nearly absolute stoppage of the blood-flow, which occurs at the beginning of the tetanus, is due to compression of this part of the muscular vascular tract; a fact which had been conjectured before, though not proved. In the second place, it is seen that the compression of the vein-trunks is alone sufficient to explain the cessation of flow observed, and that the hypothesis of a previous constriction of the arteries lasting only for a short time, in consequence of a rapid exhaustion of constrictor fibres stimulated at the same time as dilator fibres, is not only unnecessary, but is, in fact, not true; for there is no sign of any constriction of the arteries at the commencement of the tetanus, but on the contrary a steady dilatation.

Applying now the results of this experiment to the facts and curves given in my former paper, it is seen that the difference noted between the effects of a short and long tetanus simply means, that the compression of the larger veins due to the contraction of the muscular fibres is sufficient for a certain length of time to counteract the increase of flow, that would otherwise take place in consequence of the dilatation of the arteries; and that after that time, the pressure of the blood inside the veins, which has been steadily increasing, is able more and more to overcome the external pressure exerted by the contracted muscular fibres, and therefore the flow of blood from the veins steadily increases even during the tetanus itself. Again, in those cases represented by Fig. 6 of that paper[2], where the increase of flow is manifested from the very beginning of the tetanus, and where the outspurt at the onset is wanting, the explanation is easily found in the supposition, that the tetanus here was so weak as not to cause a sufficient compression of the larger veins, and that therefore the effect of the dilatation of the arteries was made manifest from the commencement. In fact, on looking over the curves representing this effect, I see that I have always noted that the tetanus was weak when a

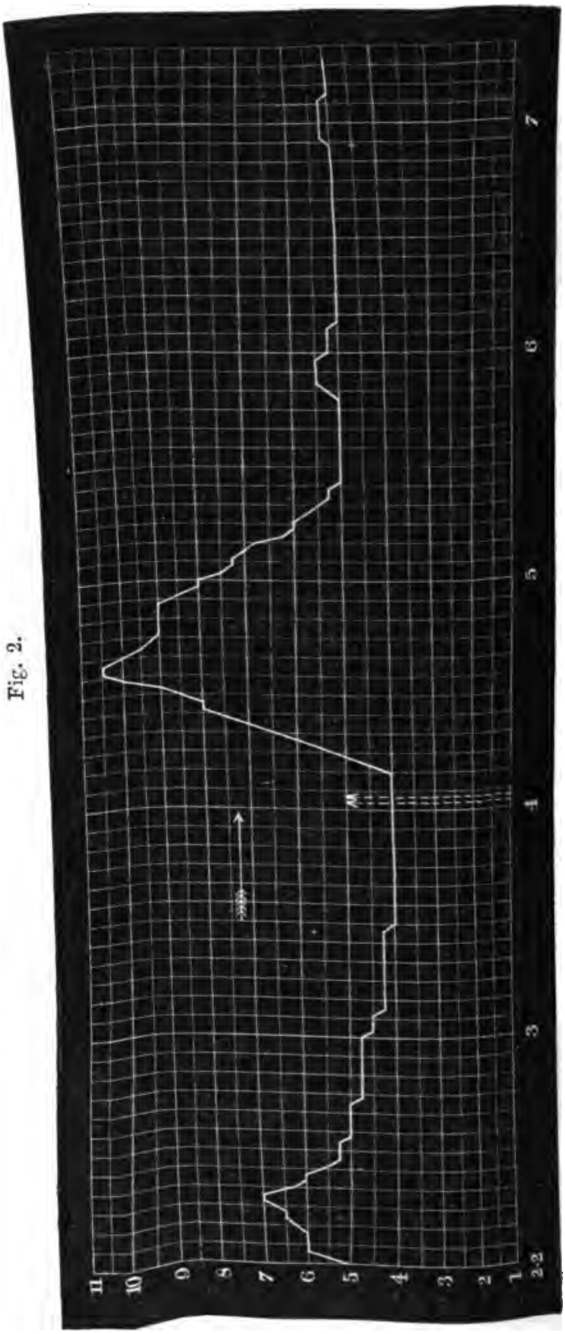
[1] *Op. cit.* [2] *Op. cit.* page 381.

curve like Fig. 6 was produced. Further, Fig. 3 in the same paper, which shows the effect of the tetanus of 0·4 seconds' duration, can only be explained on this hypothesis; for it is impossible to conceive, both that unstriped muscular fibres contract slowly, a fact which is well known, and yet that the contraction of the arteries in the extensor muscles, due to the stimulation of vaso-constrictor fibres contained in the crural nerve, is over and gone in the space of 0·4 seconds, although at the same time with the same length of stimulation the action of the vaso-dilator fibres does not reach its maximum until between 10 and 15 seconds after the stimulation is over.

The nature of the changes taking place in the vessels of the muscle, in consequence of the stimulation of its nerve, can be more efficiently studied by using larger doses of curare; for it is possible then to stimulate the nerve with even strong induction currents, without obtaining the slightest trace of muscular contraction, while at the same time the vasomotor nerves are unaffected by the curare, and so one is able to use a high power of the microscope and measure to the smallest variation the changes in calibre of the artery under observation. By the method described above, I have obtained a great number of curves showing the changes occurring under different conditions. Of these I give the following examples, in order to show the nature of the results obtained. (See Figs. 2, 3, 4 and 5.)

By studying these and similar tracings, one finds that whether the stimulation is strong or weak, long or short, there is always a certain time after its commencement during which there is no effect produced on the artery under observation; during this 'latent period,' which is of variable length, but lasts as a rule 5 or 6 seconds, there is no sign of constriction, except that, if the artery happens to be constricting when the stimulation is applied, it will continue that constriction during this period, just as if it be dilating, it will continue that dilatation, and if it be at rest, it will remain at rest. Following upon this latent period, a very rapid marked dilatation of the artery takes place, the vessel becoming crowded with corpuscles and the stream in it very full and rapid; the dilatation in some cases being so great that the diameter of the artery increases to nearly three times the size it possessed before the commencement of the stimulation

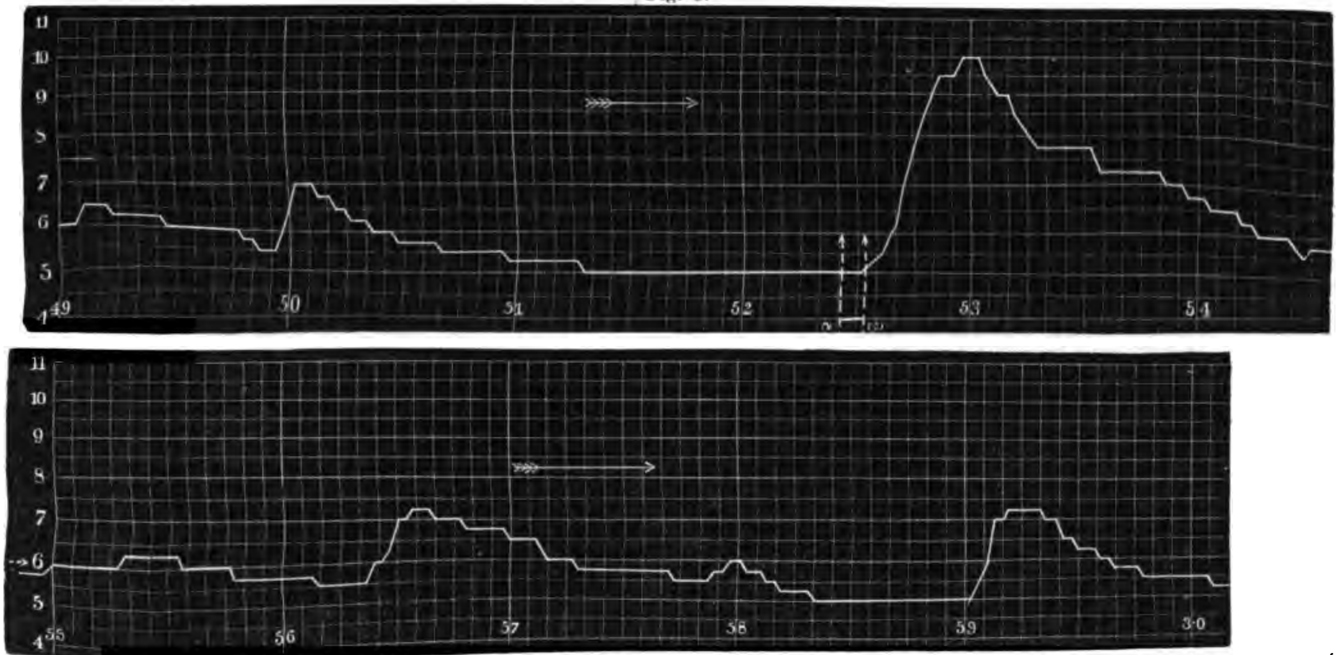
Fig. 2.



Curve showing the effect of a strong stimulation of the nerve lasting 1 second.

Measurements of the artery taken every other second. Space between the two dotted lines represents the time of stimulation. Ordinate and abscissa divided as in Fig. 1. At the commencement of the tracing one of a series of "rhythmical dilatations" is shown.

Fig. 3.

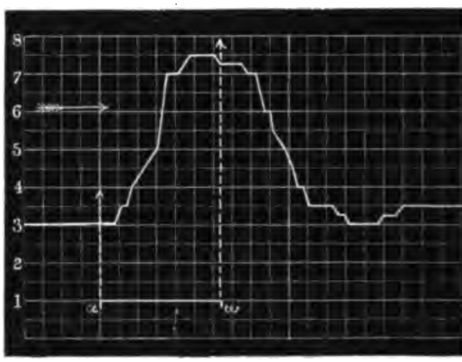


Curve showing the effect of a strong stimulation of the nerve lasting 6 seconds. The lower curve is the continuation of the upper one.

Abscissa and ordinate lines divided as in Fig. 1. Measurements of artery taken every other second. Stimulation of nerve commenced at a and ended at ω.

The curve also shows the "rhythmical dilatations" both before and after the stimulation of the nerve.

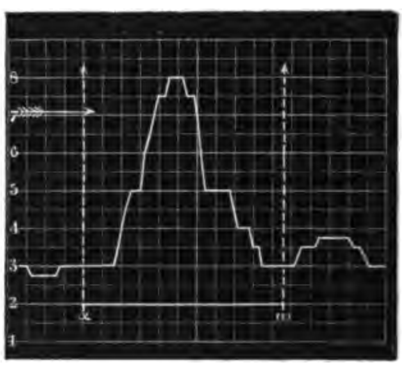
Fig. 4.



Curve showing the effect of a weak stimulation of the nerve lasting 32 seconds.

Abscissa and ordinate lines divided as in Fig. 1. Artery measured every other second. The stimulation of the nerve commenced at *a* and ended at *ω*.

Fig. 5.



Curve showing the effect of a moderately strong stimulation of the nerve lasting 54 seconds.

Abscissa and ordinate lines divided as in Fig. 1. Measurements of artery every other second. Stimulation of nerve commenced at *a* and ended at *ω*.

(see Figs. 2 and 5). The dilatation attains its maximum as a rule about 20—30 seconds after the commencement of the stimulation, and then after remaining at this point for a few seconds gradually subsides, the character of the stream again becoming normal. It is clear then, from the many exactly similar observations which I have made, that stimulation of the mylohyoid nerve causes a marked dilatation of the arteries of the muscle without any previous constriction. It is possible perchance to imagine, that the curare has made the constrictor fibres inactive and yet left the dilatator nerves intact; that this supposition will not hold good, is seen by stimulating the sciatic nerve at the same time and with the same strength of stimulation as the mylohyoid nerve, and then by observing the web and muscle at the same time, it is seen, that a stimulus which causes a dilatation in the smaller arteries of the muscle to nearly three times their original calibre, causes a constriction of the arteries in the web, so as absolutely to close their lumen, and to prevent any corpuscles from passing along. The marked contrast between the colourless absolute stagnation in the web, and the rapid full circulation in the muscle under the same conditions, is exceedingly striking. Moreover, as in the muscle it is seen that some time elapses—about 30 seconds—before the maximum of dilatation is reached, so in the web much the same time elapses before the maximum of constriction is attained. Therefore by stimulating the sciatic and the mylohyoid nerves at the same time with a strong stimulation lasting only a fraction of a second, it is easy to see, after the end of the stimulation, the progressive increase of the constriction on the one hand, and of the dilatation on the other; that is to say, that as the dilatation caused by stimulation of the muscle-nerve is not confined to the time of stimulation, so the constriction in the arteries of the web is not confined to the small time during which the electrical current is passing. Now it is impossible to consider, that the action of the vaso-constrictor nerves in the muscle can be very different from those in the web; at all events one cannot conceive, that a constriction can possibly take place in the arteries of the mylohyoid muscle, which should last so short a time as not to be observed, either during the stimulation itself in the case of a longer stimulation, or after the stimulation is over in the case of a stimulation lasting

less than one second. Besides, there is no sign of constriction when chloral alone has been given without curare. Therefore it seems to me that the supposition of Hafiz, that the vaso-constrictor nerves of muscle are very easily exhausted, is absolutely insufficient to account for the fact, that there is no sign of constriction after a stimulation lasting not longer than a fraction of a second.

Either then there are here in the mylohyoid nerve only vaso-dilator fibres, or else upon simultaneous stimulation of the two kinds of fibres the vaso-dilator always get the mastery, the exact reverse of what v. Frey[1] has observed in the case of the simultaneous stimulation of the sympathetic and chorda tympani, although agreeing according to present theories somewhat with Baxt's[2] observations on the effects on the heart of simultaneous stimulation of the accelerans and vagus nerves. There are only two cases in which I have succeeded in obtaining any satisfactory sign of constriction in the mylohyoid vessels in consequence of nerve stimulation; the first instance is the constriction mentioned below, which occurs after a long strong stimulation, the second that occurring upon reflex action, which will be discussed later on.

As I have already said, the maximum of the dilatation caused by stimulation of the nerve takes place about 30 seconds after the beginning of the stimulation, and this is true whether the stimulation lasts for a short time or a longer one, so that it is possible in the case of a short stimulation lasting only 5 seconds or less, that the whole dilatation should occur after the stimulation is over. On the other hand, as Fig. 5 shows, in the case of a longer stimulation the whole dilatation may occur during the time the current is passing, so that when the stimulation is ended, the artery under observation is found to have regained its normal character; that is to say, the extent of the dilatation caused by stimulation of the nerve depends rather on the strength of that stimulation, than on the duration of it. It is not possible however with the same strength of stimulation, however strong that may be, to make the dilatation last for any length of time; although I have succeeded in keeping the artery under observation in a state of maximum dilatation for

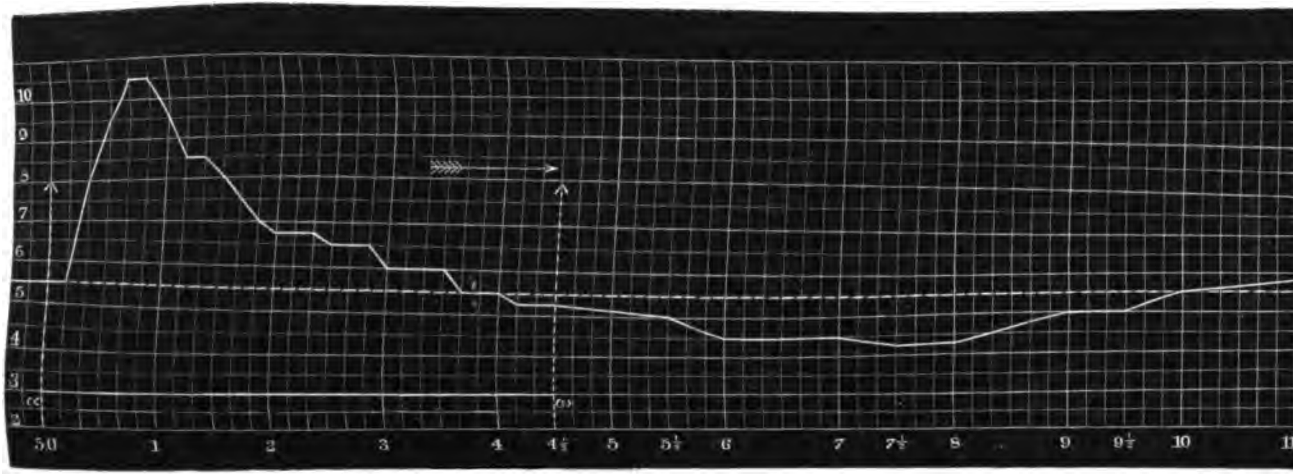
[1] *Ludwig's Arbeiten*, 1876. [2] *Ibid.* 1875.

as long a time as 5 minutes, by commencing with a weak stimulation, and continually and very gradually increasing the strength, whenever the dilatation showed signs of diminishing; on the other hand, in the case of a strong stimulation of unvarying strength lasting 4½ minutes, it is seen (Fig. 6) that before the end of the stimulation the calibre had returned to the normal size, the dilatation caused in fact being very much the same in extent as would have been caused by a stimulation of the same strength, lasting a much shorter time. The curve however shows another circumstance of great interest, which occurs as a rule after any stimulation that has been long enough and strong enough, viz. that upon the cessation of the stimulation, the artery not only does not dilate but steadily continues to diminish in calibre, until at last, some time after the end of the stimulation, it has reached a size considerably less than that which it possessed before the beginning of the stimulation; after remaining at this minimum for a short time, the vessel again gradually returns to its normal size or even slightly above it. We see then, that whereas in the case of the web a long and strong stimulation of the sciatic nerve causes constriction of its arteries, followed after the stimulation by dilatation, so here the same cause produces dilatation of the arteries of the muscle, followed after stimulation by constriction. One would rather then imagine that, as a consequence of any stimulation of such a nerve as the sciatic, constriction of the arteries of the skin is accompanied by dilatation of those of the muscles, and dilatation of the skin-vessels by constriction of those of the muscles. How far in this way a compensation takes place between the two vascular areas of the skin and muscle in any part of the body, will depend upon the degree in which the two areas are supplied by the nerve, whose action is being investigated.

A similar occurrence to this secondary constriction has been observed by Hafiz[1]. He noticed that the dilatation of the arteries in muscles caused by a strong stimulation of the upper portion of the spinal cord was followed by a very marked constriction of them; and in his paper this seems to me to be the only satisfactory constriction of the muscle arteries that he observed; for, although he says that he has sometimes seen a more or less

[1] *Op. cit.*

Fig. 6.



Curve showing the effect of a strong stimulation of the nerve lasting 4½ minutes.

The ordinate line divided as in Fig. 1. Each of the divisions of the abscissa line represents 10 seconds. Stimulation of the nerve commenced at *α* and ended at *ω*. Measurements of the artery taken every 10 seconds until the end of the stimulation, then every minute or half minute. For some 5 minutes before the stimulation commenced the diameter of the artery had measured 5 or 5·5, the fluctuations in its size being very slight.

temporary constriction of the muscular branches of the ulnar artery, previous to the marked dilatation caused by stimulation of the spinal cord—and upon this he founds his assumption that the vaso-constrictor nerves of the muscle arteries are exceedingly easily exhausted—yet he expressly says, that he has never seen the slightest trace of this constriction in curarized animals, although at the same time there is marked constriction in other arteries, and also, that as a rule stimulation of the upper portion of the spinal cord causes no constriction of the muscle arteries, but, on the contrary, causes a great increase in the amount of blood flowing from the cut surface of the muscle. Hence it seems to me plain, that in those cases where he noticed constriction of the muscle arteries upon stimulation of the spinal cord, there must have been at the same time a contraction of the muscle; and that therefore, whichever of his different methods was the one by which he noticed the fact of constriction, the mere presence of a simultaneous contraction of the muscle must have made it very difficult, to say the least, for him to have been sure that what he observed was really due to the stimulation of vaso-constrictor fibres of the muscle arteries. In the case of a curarized frog, stimulation of the medulla causes a decided dilatation of the arteries of the mylohyoid muscle without any previous constriction, although at the same time the arteries in the web are strongly contracted; and if the mylohyoid nerve be first cut, then stimulation of the medulla remains without any marked effect, there being certainly no constriction although possibly a very slight dilatation produced.

4. *Effects of reflex stimulation.*

As I have mentioned in my former paper, it does not follow that, because contraction of a muscle is accompanied by dilatation of its arteries when the muscle-nerve is artificially stimulated, the same thing should occur in the case of a contraction of the muscle caused by voluntary or reflex stimulation. As it is not possible in the frog to examine the muscle and note the effects of voluntary muscular contraction, one is compelled to confine oneself to the question, what is the effect of reflex action on the arteries of the mylohyoid muscle.

As is well known, stimulation of a sensory nerve causes a great increase in the blood-pressure of the larger arteries, owing to a reflex constriction of a large number of the smaller arteries in the body. A very indirect proof, that the arteries of muscles do not partake in this previously supposed nearly universal constriction, is given by Hafiz; whether however the muscle-arteries simply remain unaffected, or are partially constricted, or whether they absolutely dilate upon stimulation of a sensory nerve, his method of observation is insufficient to show; he simply proves, that all blood channels are not occluded, when by different means he causes a great rise of pressure in the carotid; he concludes thereupon, that the open paths for the blood stream are situated in the muscles. By my method of observation, I was able to test how far this theory is true for the frog, at the same time being able to control the effect of the stimulation, by observing simultaneously the circulation in the web and the muscle. The nerves, whose central ends I stimulated with varying strengths and durations of stimulations, were the two sciatics, the vagi, and the opposite mylohyoid, and in no case was there any dilatation of the arteries under observation to be seen; either no change at all was produced, or else together with a diminution in the rapidity and fulness of the blood stream a slight very gradual constriction of the artery was observed. At the same time it was seen, that the vessels of the web constricted notably when those in the muscle remained unaltered, and that in the case of stronger stimulation where there was a very slight constriction of the mylohyoid arteries to be observed, those of the web were absolutely occluded and the whole circulation there stopped; this was true, not only when the central ends of the sciatic and vagi nerves were stimulated, but also when the nerve made use of was the opposite mylohyoid; it being no more possible to produce any marked effect on the muscle arteries by the use of this latter nerve, than by the use of any other sensory nerve. It seems then clear, that stimulation of sensory nerves, while causing a marked constriction in the arteries of the web, does not affect the arteries of the muscles to any great extent in either one way or the other, what effect there is being rather in the direction of constriction than

dilatation. That there is a slight constriction caused seems probable from the fact, that although if the muscle-nerve is left intact stimulation of an ordinary sensory nerve never produces a trace of dilatation in the artery under observation, but either no effect or else a slight constriction, yet when the muscle-nerve has first been cut and a sufficient time elapsed for the circulation to have recovered its normal character, then stimulation of an ordinary sensory nerve sometimes causes a slight dilatation of the muscle-arteries, owing clearly to the greater amount of blood sent through the muscle in consequence of the marked constriction occurring in other parts of the body; therefore, even in those cases where the stimulation of a sensory nerve appears to produce no effect on the calibre of the muscle-arteries, this very fact shows, that in reality the vaso-constrictor fibres in the muscle-nerve must have been thrown into action to such an extent as to counteract the dilatation, that would otherwise have taken place in consequence of the increased flow of blood through these vessels.

From this fact then, that stimulation of a sensory nerve does not cause dilatation of the vessels of the muscle, it would seem to follow that a contraction of the muscle caused by reflex action is not accompanied by a stimulation of the vaso-dilator nerves of the muscle. Before however one can speak with certainty on this point, it is necessary to make sure that there is no particular locality, stimulation of which will produce dilatation of the arteries in question. We know already a considerable number of local reflex dilatations of vessels; thus stimulation of the central ends of the saphena and great auricular nerves of the rabbit causes a dilatation of the saphena artery and of the median artery of the ear respectively (Lovén)[1], and in the case of the submaxillary gland, stimulation of the tongue or central end of the lingual nerve causes a reflex dilating action of the chorda tympani (Vulpian). This latter case seems especially to shew, that the same cause which calls the function of an organ into play calls into action the vaso-dilator nerves of that organ; therefore applying this to the case of the mylohyoid muscle, it is clear that the most likely method to obtain a reflex dila-

[1] *Ludwig's Arbeiten*, 1866.

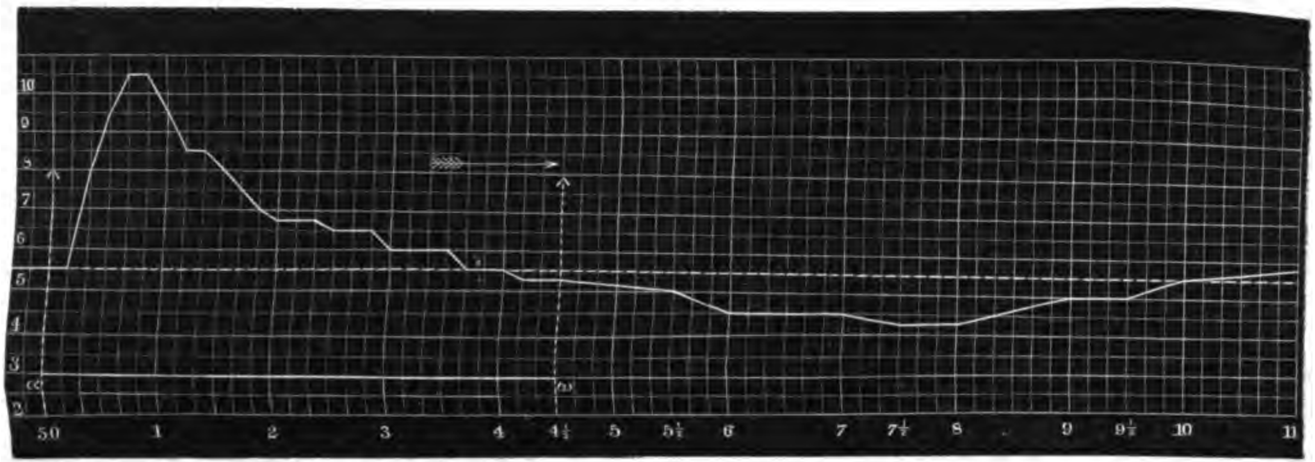
tation of its vessels is to apply a stimulus to those places, where it is easiest to obtain a reflex contraction of the muscle. One must then first find out, where these most favourable spots are; now the two mylohyoid muscles are essentially muscles of respiration and deglutition, and by first removing the cerebrum and optic lobes in a non-curarized frog, so as to obtain the phenomena of reflex contraction in the purest manner, it is easily seen, that a small piece of blotting paper dipped in 5 per cent. solution of acetic acid placed either at the opening of the glottis or œsophagus, immediately causes a strong reflex contraction confined to these muscles and their neighbours, while the same stimulus applied to other parts of the body has no effect as far as these two muscles are concerned. Stimulation here then causes a reflex contraction of these muscles, is this accompanied by a reflex dilatation of the arteries or not? This question must, I think, be answered in the affirmative, for although I have not succeeded in obtaining as clear and constant evidence of dilatation by stimulation here, as by stimulating the muscle-nerve itself, yet I have sometimes seen decided dilatation of the vessel under observation on the application of a stimulus to these parts; and as a rule this much can be said, that after the entrance of the œsophagus or glottis has been stimulated in any way, the artery measured is for some time afterwards slightly larger, and the stream in it certainly fuller and more rapid than before the stimulation. The most satisfactory and most pronounced dilatation that I have seen has been, when the glottis was opened and a blunt instrument such as a seeker passed in as far at least as the vocal cords; in these cases I have seen a distinct dilatation take place not only after the instrument has been withdrawn, but also while it was still held in position within the opening of the glottis. At present therefore I am inclined to think that the arteries of the mylohyoid muscle of the frog behave in accordance with what may prove to be a general law, viz. that stimulation of a sensory nerve causes dilatation of the smaller arteries of that part, with which it is in functional relation, and constriction more or less marked of the remaining smaller arteries of the body. As it is however very advisable to determine whether the

vascular system of the muscles of mammals conforms to the law of reflex action here laid down, before speaking positively on the subject I will defer further discussion, until the completion of certain experiments on curarized mammals, by which I hope to obtain a solution of this question; for I cannot help thinking, that I have laid too much stress upon the single curare experiment mentioned in my former paper[1], and that it is very improbable that curare should destroy the action of vaso-dilator fibres in the case of mammals, while leaving them intact in the case of frogs, especially as Hafiz mentions, that in many of his experiments he made use of curare, and yet does not lead one to conclude, that in these cases the dilatation effects noticed by him in the vessels of muscles upon stimulation of the cord were absent, although he expressly states that the preliminary constriction was always wanting. Further it is not possible even by large doses of curare to paralyse the dilator fibres in the mylohyoid nerve of the frog, for I have purposely given large doses of curare at one time and also many times the usual dose by means of injections repeated at intervals, and yet have always found that the vessels of the muscle dilated in response to stimulation of the nerve.

As Claude Bernard has described a dilatation of the branches of the facial artery upon stimulation of the mylohyoid nerve in the case of the mammal, I have experimented in the same manner upon two other muscles of the frog, viz. the abdominal portion of the pectoralis major and the lateral portion of the rectus abdominis muscles, and have seen in each case dilatation of their arteries upon stimulation of their respective nerves. As however the preparation of these muscles is not so easy as that of the mylohyoid, I have not as yet extended my experiments upon their vasomotor nerves. I have however seen enough to justify the assumption that the phenomena described in this paper are not confined to the mylohyoid muscle. In the case of the tongue I am inclined from the few experiments I have made to agree with v. Frey[2], that stimulation of the glossopharyngeal, rather than the hypoglossal nerve, causes vascular dilatation here, as also Vulpian has proved for the mammal.

[1] *Op. cit.* page 372. [2] *Op. cit.*

Fig. 6.



Curve showing the effect of a strong stimulation of the nerve lasting 4½ minutes.

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[1] *Ludwig's Arbeiten*, 1866.

reversed during each of these shortly lasting dilatations, and at the end the artery remains constricted and the corpuscles stationary as in the first case; if, as sometimes occurs, probably from some peculiarity in the tension of the muscle, the corpuscles are moving in the reverse direction, i.e. from the veins to the arteries, during the constriction of the vessel, then with each dilatation the motion is changed to the normal direction; sometimes the artery under observation is found to be absolutely constricted directly after the removal of the heart; this I have only noticed in three cases when the heart had been cut out previous to the section of the muscle nerve, and in each case subsequent section of the nerve was without effect, the artery remaining in the same state of absolute constriction. Upon stimulation of the nerve, either when the artery is at the end of its constriction or while it is still constricting, a marked dilatation of the vessel is often seen to take place, the corpuscles moving in a direction the reverse of their motion during constriction; the amount of this dilatation, though sometimes as great as the doubling of the calibre the vessel possessed just before the stimulation, is yet always less than that produced by the same stimulation when the full circulation is present, and is often sufficient only to enlarge the vessel up to that size, which might be considered the normal one previous to the removal of the heart. In one of the three cases above mentioned where the artery remained absolutely closed after section of the nerve, the unstriped muscular fibres could be clearly seen projecting along the edge of the artery and the inner lumen was clearly marked by two lines nearly touching, so that by using a power, with which every space on the micrometer scale corresponded to $\frac{1}{244}$ m.m., the whole vessel measured 5, each muscular wall representing 2 and the inner lumen 1. Upon stimulation of the muscle at the point of entrance of the nerve, the hitherto closed vessel was made to open and finally after two or three stimulations the size of the vessel had reached 7, of which the inner lumen represented 5 and each muscular wall only 1: at the same time the separate projections of the contracted muscle fibres nearly disappeared, so that the outer edges of the vessel were now almost as smooth as those of the inner lumen. As the vessel dilated two corpuscles

made their appearance coming from the venous side, which when the vessel again began slowly to constrict moved again towards the veins; as long as the observation lasted the artery now remained open, the inner lumen never becoming less than 3.

The foregoing experiment does not enable us to decide between the two rival theories, which have been put forward to explain vaso-dilator action, for, although on the "active dilatation" theory it is easy to see how the stimulation of the peripheral ends of vaso-dilator fibres might occasion a dilatation of an artery, while at the same time the removal of tonicity implied by the section of the nerve was unable to do so; yet it is also quite conceivable, that the section of the nerve, i.e. the removal of the action of some cerebro-spinal vasomotor centre, was unable to produce any effect, because, in consequence of the absence of the blood-supply, the tonic influence of the peripheral local vasomotor centres was so much increased, that this alone was able to hold the vessel in a state of constriction; while, on the other hand, stimulation of the peripheral end of the nerve caused the vessel to dilate, because the action of the peripheral local centres was thereby inhibited. As an alternative to this view, it may be urged, that possibly the mylohyoid nerve contains only a few vaso-constrictor fibres, and that the majority of these fibres take some other course, as for instance directly along the vessels of the muscle themselves, so that section of the nerve in the case cited was unable to produce any effect, because the supposed other constrictor fibres were thrown strongly into action by the stimulation of the cerebro-spinal vaso-motor centre, in consequence of the absence of its blood-supply; while stimulation of the peripheral end of the nerve removing the action of all constrictor fibres allowed the artery to relax; and as a proof of the existence of these fibres, the fact might be urged, that it is ordinarily possible to produce a greater dilatation by stimulation of the nerve, than by section of it, and therefore that the mylohyoid nerve does not contain all the constrictor fibres of the arteries; also the varying length of time that dilatation lasts after section of the nerve would be explained by supposing that sometimes more sometimes less constrictor fibres are contained in the nerve itself. Against this possibility however is the fact, that stimu-

lation of the upper portion of the spinal cord is absolutely without effect when the mylohyoid nerve has first been cut; also, if there were nerves of this character situated upon the vessels themselves, it seems reasonable to suppose, that direct stimulation of an artery, by not only stimulating them, but also stimulating the muscular coat of the vessel itself, ought to produce a marked contraction of the vessel. I therefore performed a series of experiments on the direct stimulation of the muscle arteries with the following results.

In order to confine the stimulation to the small artery under observation, and at the same time not to injure the vessel or the muscle by the application of the electrodes, I attached to each of the platinum points a long, thin, very finely pointed strip of tinfoil, and arranged so that I could place each tinfoil point so as just to touch the muscle at any particular spot I desired. In order to use the same magnifying power as in my other experiments, I at first placed these electrodes underneath the muscle and moved them upwards, until I could see on looking through the microscope that their points just touched the muscle at the right places; finding, however, that it was very difficult to be sure of placing them rightly in position in this way, I discarded the higher object-lens, and in most of my observations made use of a power, by which every space of the micrometer scale corresponded to $\frac{1}{80}$th m.m. With this power I was able to insert the tinfoil strips between the lens and the muscle, and could therefore easily manipulate, so that the points alone of the tinfoil strips touched the muscle wherever I pleased. Again seeing that, except with a very weak current, the contraction of the muscular fibres between the electrodes is necessarily so strong, as to prevent at all accurate measurement of the artery under observation during the stimulation itself, I adopted the plan of limiting the time of stimulation to one second or less, and to prevent the possibility of the tinfoil points holding the muscle in its contracted position, I lifted them rapidly from the muscle at the end of the stimulation; by this means I was able to measure accurately the calibre of the artery in less than ten seconds after the commencement of the stimulation, a time sufficiently short, so it seems to me, to make certain, whether the primary effect of the stimulation was a constriction or a dilata-

tion of the vessel. By these methods I found that, whether the tinfoil points were placed so that the current passed longitudinally along the axis of the artery, or transversely across that axis, with a stimulus so weak as to cause a contraction of the muscle not sufficient to interfere with the measurement of the artery, the vessel was seen to dilate steadily from the commencement of the stimulation, without any sign of previous constriction, the dilatation occurring during the stimulation itself and continuing after it was over, if the time of stimulation was short enough; in fact, the dilatation produced was quite similar to that caused by stimulation of the nerve; in the case of a stronger stimulation lasting less than one second, the artery was found to be dilated as soon as it could be measured again, and this dilatation continued until it had reached its maximum about 30″ after the stimulation, the maximum being as great as could be produced by stimulation of the nerve; upon still further increasing the strength of the stimulation, a point was at last reached, when instead of an increasing dilatation of the vessel after a stimulation of less than one second duration, the artery under observation was found to be most markedly constricted as soon as the measurement was again possible, and this constriction so caused was by no means temporary, but instead lasted for much the same length of time after the stimulation, as the constriction caused in the arteries of the web by the same mode of procedure, the vessel remaining nearly absolutely closed for some time and difficult to see, and then gradually reopening, until at last it reached a size decidedly greater than before the stimulation, although not so great as was previously obtained by using a slightly weaker strength of current. The dilatation that follows upon a weak or moderately strong stimulation occurs whether the nerve has been previously cut or not. Frequently when the electrodes have been placed transversely, so that the current crosses the artery, it is seen, that the dilatation caused by stimulation is confined or nearly confined to that particular part of the vessel between the electrodes, a most marked bulging taking place at this spot, the rest of the artery and the neighbouring vessels being hardly if at all altered; and then, upon stimulating with a much stronger current, this part of the vessel alone is constricted

to nearly absolute closure, the rest of the artery both in front of and behind the affected piece being somewhat dilated, with a more rapid full stream on the proximal side and a full sluggish stream on the distal side; this local constriction being followed by a decided local dilatation of the same part. The arteries some little distance removed from the electrodes are quite unaffected, remaining of the same calibre throughout. I am unable as yet to say in what way the change takes place from dilatation on stimulation to constriction on stimulation, although, from what I have noticed in one case, the sequence of events seemed rather to be, that up to a certain strength of current dilatation alone was observed, then with a very slightly stronger current a brief constriction quickly followed by dilatation took place, and with the increase of the strength of the current the constriction became more lasting and more manifest, the subsequent dilatation occurring later, until a strength was reached, which caused a long-enduring very marked constriction of the vessel.

From these experiments two things appear to me clear, 1st, that direct stimulation of an artery does not necessarily cause that artery to contract, but may cause it to dilate; 2nd, that the assumption of Hafiz, that the unstriped muscular fibres of the arteries of muscle are very easily exhausted, is again proved to be untenable; for, if this were the case, one would expect to find constriction of those vessels most marked upon weak stimulation, and dilatation of them upon strong stimulation, whereas the reverse is the case.

Seeing then, that in the case of the arteries of this muscle it is possible to cause dilatation by nerve stimulation, after the circulation through the muscle has been removed, and also, that direct excitation of the artery causes it to dilate if the stimulation is not too strong, and to contract if it is very strong, one seems driven to seek for some other explanation of vaso-dilator action than the ordinarily accepted theory of inhibition; if, for instance, one could assume, that an unstriped muscular fibre possesses the power of contracting in two directions, longitudinally and transversely, so that in the one case the fibre becomes thicker and shorter, and in the other thinner and longer, then the difference between vaso-constrictor and vaso-dilator nerve-

fibres would consist in the assumption, that in the first case the nerve-fibre terminates in the muscle in such a way, as to cause upon its excitation a contraction in the direction of the long axis, and in the second case a contraction in the direction of one of the short axes of the muscle-fibre.

However, upon the supposition, that dilatation of an artery is caused not by the removal of contraction but by contraction in another direction, it is reasonable to assume that, just as it is possible to cause constriction of arteries by nerve stimulation in a tissue that has been removed from the body, so it should be possible to cause dilatation of the arteries of the mylohyoid muscle by stimulation of its nerve, when the muscle has been entirely removed from the body. In all my attempts to obtain dilatation in this way I have completely failed; stimulation of the nerve of the isolated curarised muscle, which has been separately pinned out under the microscope, producing no effect whatever upon the size of the muscular arteries. I am inclined therefore at present to imagine, that it is not possible to produce dilatation of an artery from which all internal pressure has been removed, and that in the cases where dilatation was caused after removal of the heart, there was really sufficient blood-pressure left in the whole vascular system to cause the amount of dilatation observed upon the hypothesis of inhibitory action alone. One must then explain the dilatation caused by direct stimulation of an artery as due to excitation of the endings of the vaso-dilator nerves, while the marked constriction that occurs upon very strong direct stimulation would be due to the excitation of the circular muscle fibres themselves overpowering the action of the dilator fibres. Although therefore for the present I do not deem the evidence strong enough to overthrow the accepted theory of inhibitory action, yet it might possibly be worth while to investigate, whether between the simple unspecialized contractile protoplasm of the amœba, capable of contraction in all directions, and the highly specialized striated muscle fibre, intermediate forms of contractile tissue may not be found, in which the power of contraction is limited along certain axes; and whether the smooth unstriped muscular fibre may not represent one of these intermediate stages.

NOTE ON THE EFFECT OF HEAT ON THE HEART'S ACTION IN THE CHICK. By Professor CLELAND, *Galway*.

PERHAPS it is not so generally known as it might be that the heart's action in the early stages of development of the chick is very easily accelerated by heat, and that this can be exhibited with the utmost facility on a watch-glass.

I may state that in examining embryos of 24 hours and upwards, I find it best not to subject them to the action of saline solutions, but to clean them as rapidly as possible, and examine them with no more water present than is necessary to preserve the natural degree of moisture. In this way a better view of anatomical details is obtained than by immersion in fluid, and the embryo may be kept alive for a considerable time; as will be seen from the following note of the effect of heat in a particular instance.

The egg was 52 hours hatched; the sinus terminalis was partially filled with blood, and the heart colourless. The embryo was floated out on a watch-glass, and the water poured off so as to leave the embryo adherent. The heart beat regularly at 36 beats per minute for some time. Laid on the cold table for a moment, it stopped; but it began again to beat when approached to the lamp. By continuing to hold it near the lamp, it was made to beat at the rate of 96 per minute. Afterwards, when the heart again stopped, a longer approach to the lamp became necessary to reestablish the beating. But rhythmic contraction could be detected up to forty minutes after the first observation. At that time, approach to the lamp produced a faint movement at the rate of 100 per minute, which lasted not more than 15 seconds; and after that, excitation ceased to have any effect. It is interesting to note that in the chick, where one homogeneous structure apparently combines the rhythmic impulse, excitability by artificial irritation, and contractility, the effects of heat are the same as on fully formed hearts supplied with ganglia.

NOTE ON MR GORDON'S PAPER 'ON CERTAIN MOLAR MOVEMENTS, ETC.' *Journal of Anatomy and Physiology*, Vol. XI. p. 533.

No doubt Mr Gordon's general explanation of the phenomenon he has observed is correct as far as it goes; but the actions and reactions between the heart, the moving blood and the walls of the blood-vessels are so complicated that any rigorous discussion of their effects would be both very difficult and very lengthy. The simplest way of treating the mechanical problem seems to be the following.

During systole a certain quantity of blood is transferred from the heart to the great vessels. As the abdominal aorta and its branches constitute an important part of the arterial system and are at a comparatively considerable distance from the heart, the effect of this transfer is to cause the centre of gravity of the body to be somewhat nearer to the feet immediately after systole than before it. Now as no internal actions can alter the position of the centre of gravity in space, the whole body must move during systole—if no external forces are acting upon it—in the direction in which the upper portion of the trunk is pointing, so that the position of the centre of gravity in space may be unchanged.

The motion of the body at any moment must be proportional to the excess of downward over upward transference of blood at the time. The curve representing it must therefore resemble the aortic pulse curve, though the correspondence is probably not so exact as Mr Gordon supposes.

The simplest way of getting an accurate tracing would probably be to suspend the body as Mr Gordon does, and to attach the tracing point rigidly to the skull by holding the rod which carries it firmly between the teeth.

Trinity College. COUTTS TROTTER.

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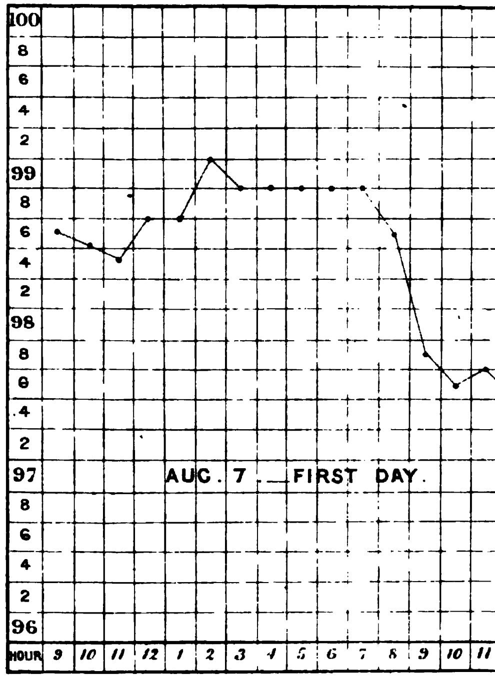
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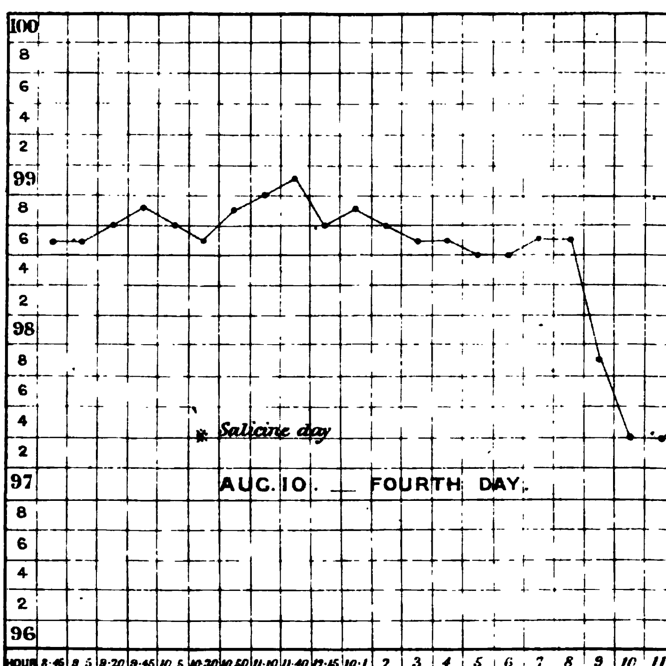
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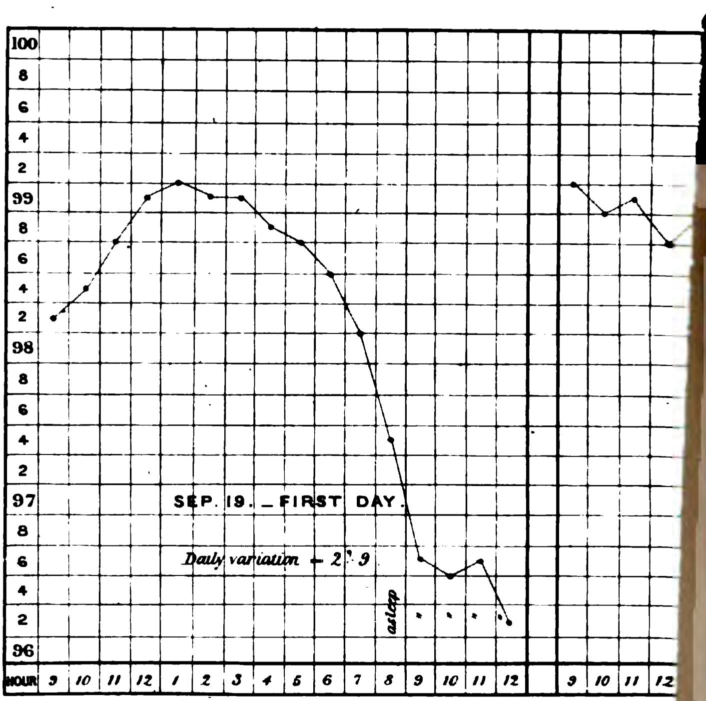
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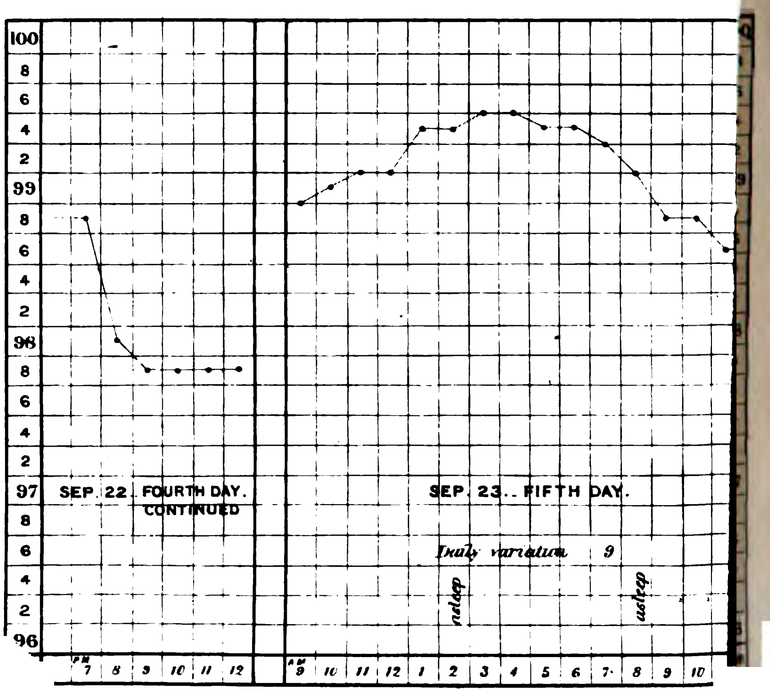
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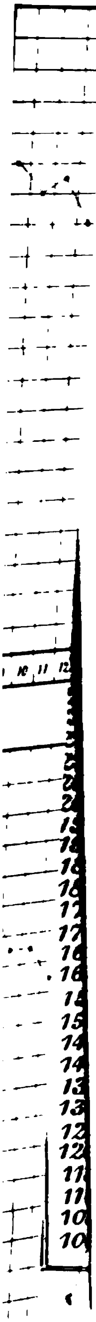

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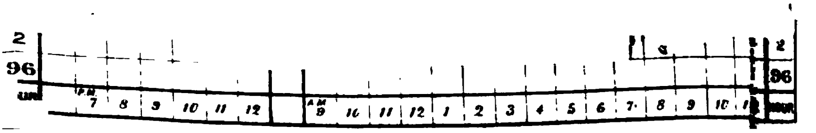
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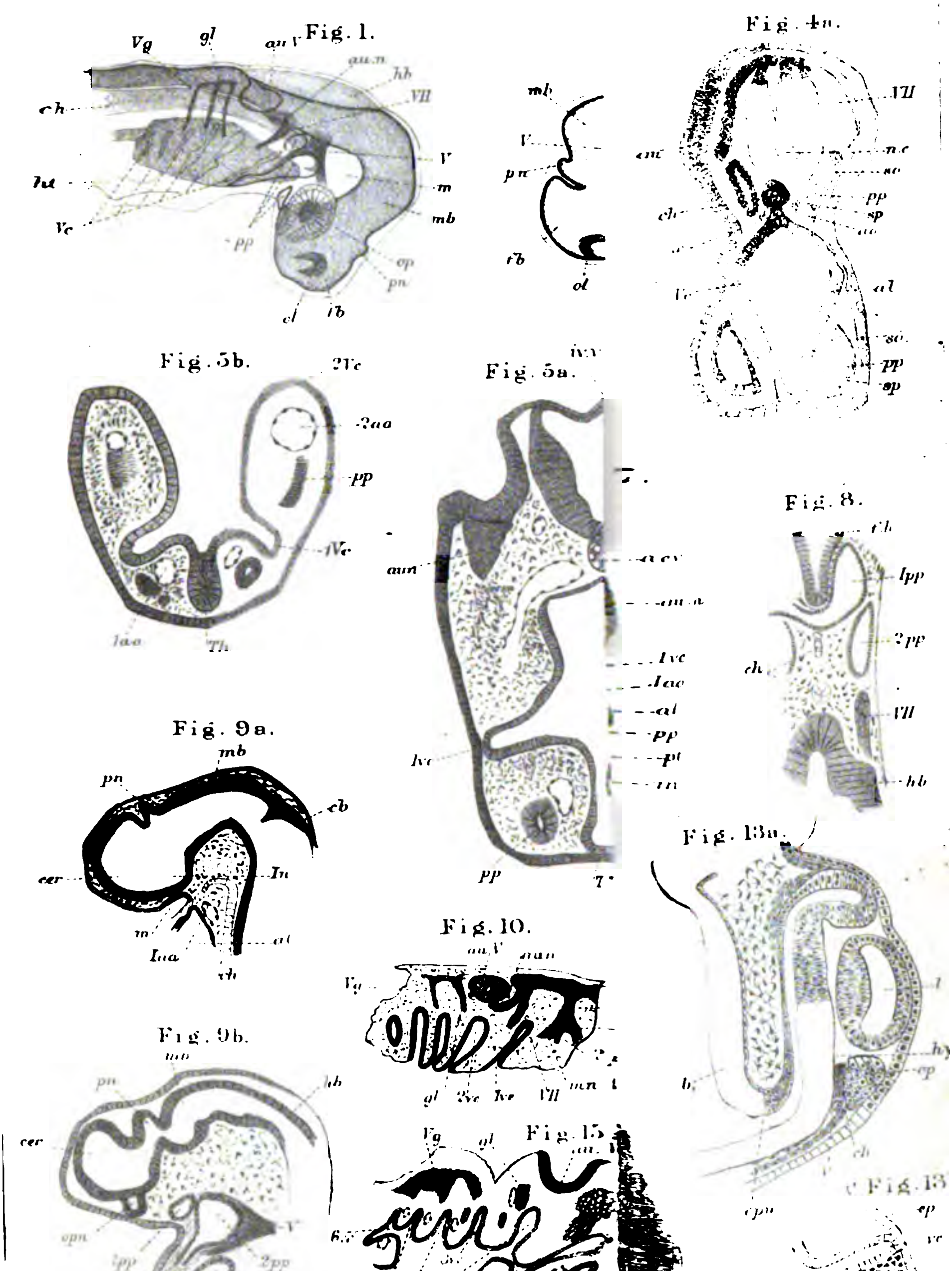

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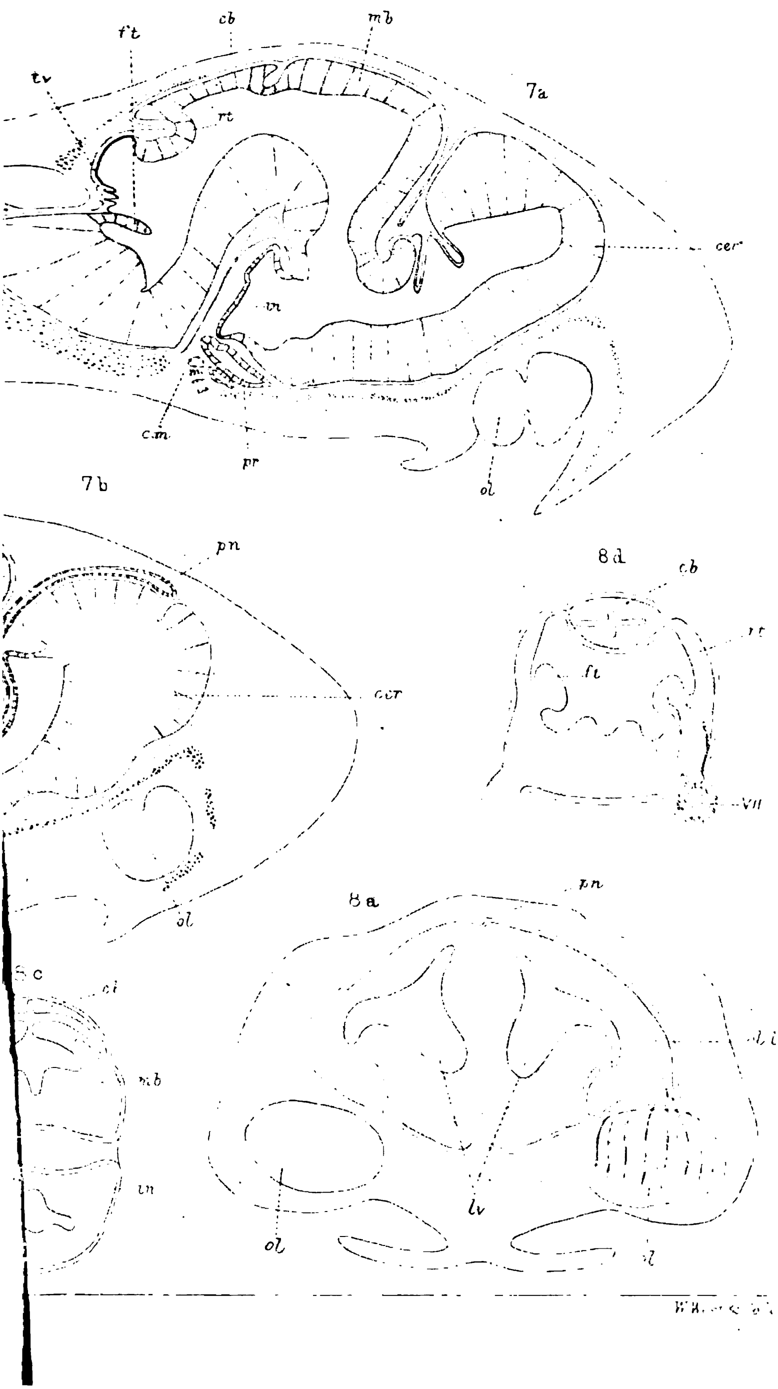
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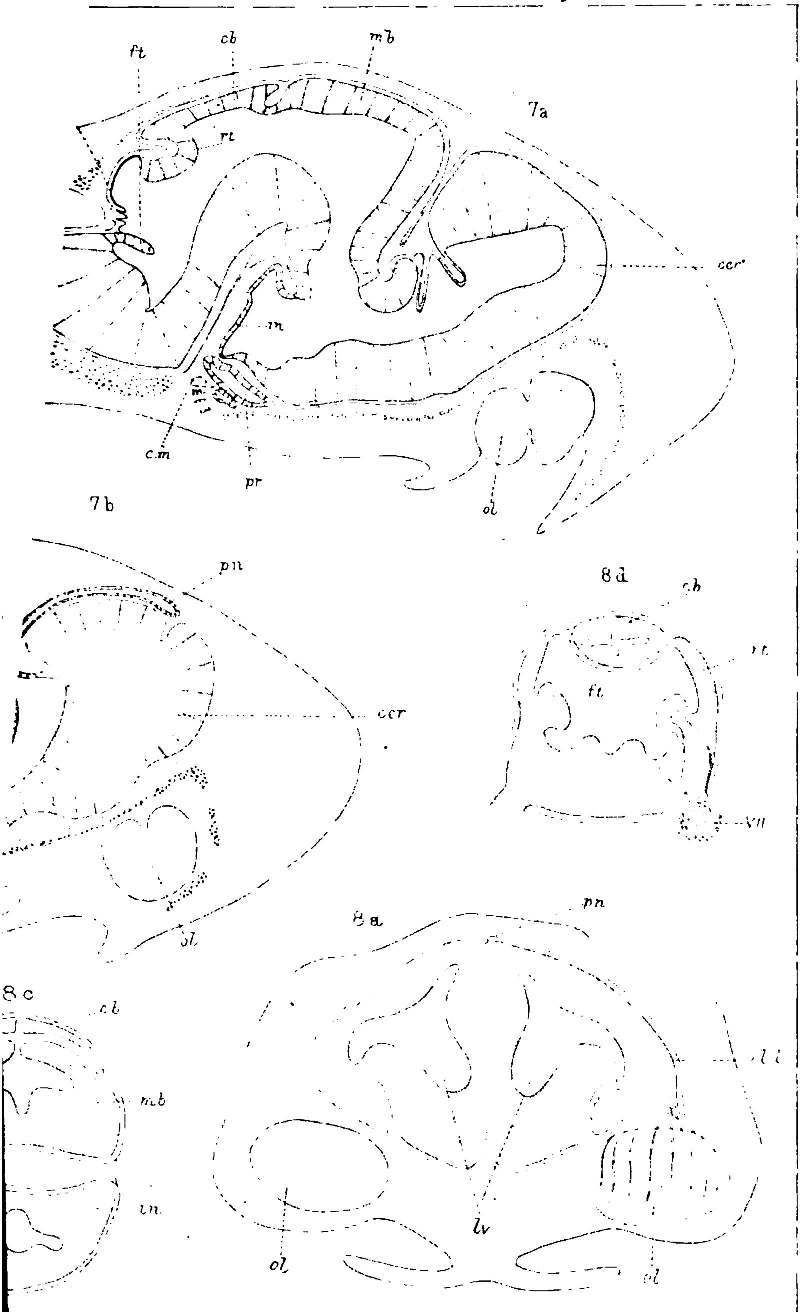
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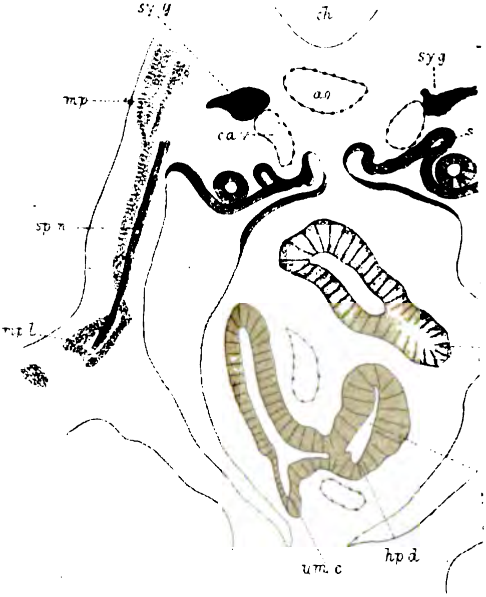

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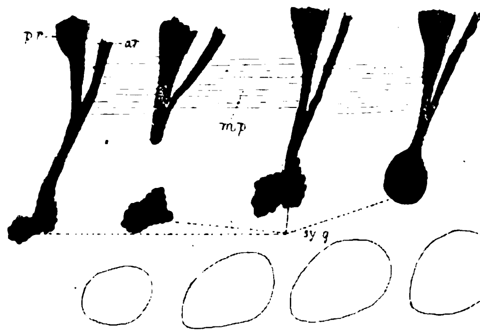

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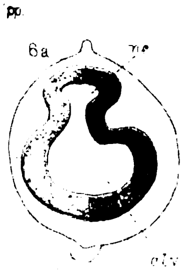

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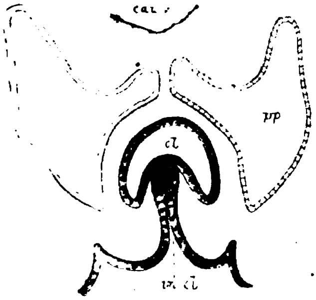

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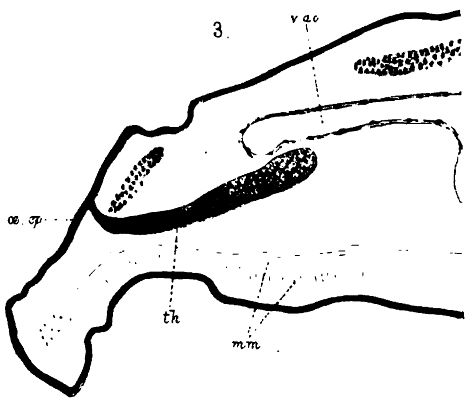

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